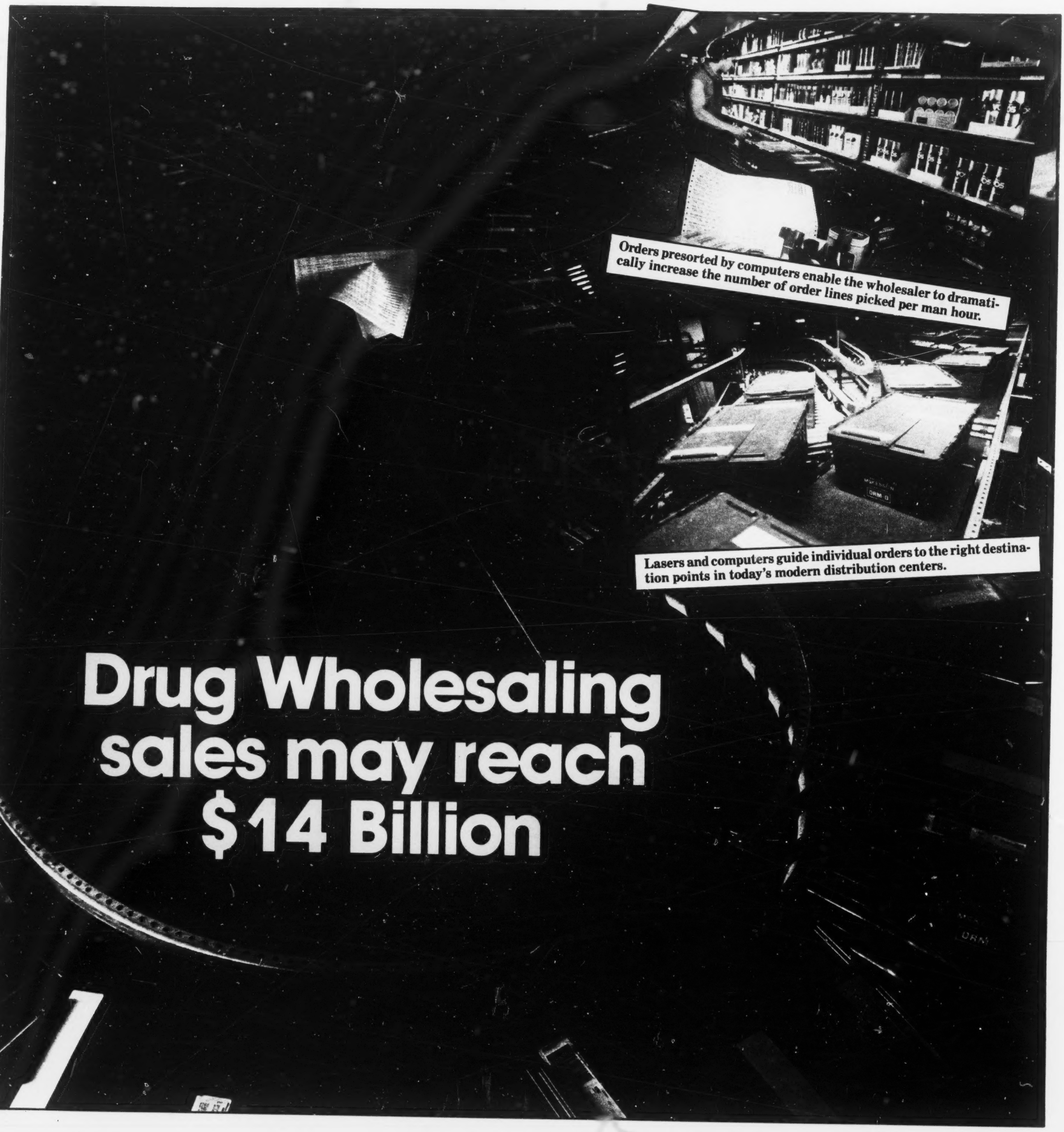
1984 Annual Report of the Wholesale Drug Industry



Orders presorted by computers enable the wholesaler to dramatically increase the number of order lines picked per man hour.

Lasers and computers guide individual orders to the right destination points in today's modern distribution centers.

Drug Wholesaling sales may reach $14 Billion

The wholesale drug industry in 1984 is continuing to expand dramatically—both in product lines carried and in types of customers serviced.

The major companies are either expanding their product lines to achieve greater sales penetrations from their current customer base or are studying the possibilities of such an expansion.

There is an intense effort to attract new customers, specifically hospitals, nursing home suppliers, HMO's and other similar accounts. There is some trend toward consolidation of facilities so that companies can achieve the operational efficiencies that come from pumping a higher sales volume through single centers. And there is a major thrust in automating programs so that productivity savings can be realized.

There is a growing emphasis on developing voluntary or cooperative advertising customers so that independent retailers can be armed to compete on a more aggressive level with the chains, and there is a great amount of energy being devoted to the development of new merchandising programs that will support the retailer as he or she expands in-store mix of products, particularly in such hot growth categories as home health care convalescent aids.

There is also a new onslaught of "acquisition fever" sweeping the industry as price-earnings multiples return to more acceptable purchasing levels and as growth-minded tigers such as FoxMeyer knuckle down to the business of spending the capital they raised from going public.

Almost all of the companies interviewed by *Drug Store News* for this report were broadening their product line base in 1984. McKesson has developed a full-line stationery and home and school supplies program as well as a full line of medical-surgical supplies. It was adding such new lines as pet care, reading glasses, hosiery, hair lotions and fragrances to its mix.

Bergen Brunswig was rolling out a stationery program and filling in products for such categories as watches, pantyhose, batteries, baby care, lawn chairs and other seasonals, etc. McPike was expanding its selection of home health care and durable medical equipment, as well

Continued on page 17

1984 Annual Report of the Wholesale Drug Industry

Continued from page 15

as continuing its emphasis on fragrances.

Amfac was studing the possibility of product-line expansions. Durr-Fillauer was diversifying into stationery and school supplies. Drug Service, a division of Synergex, which only a few years ago expanded heavily into H&BA products, was investigating a wide variety of other product expansions, including electronics, candy, tobacco and food. Ketchum Distributors had completed the rollout of 16 new merchandising departments and was preparing to launch a second phase of rollouts.

Just about everyone was developing or introducing home health care programs.

"You know that because of automated order/entry systems, most retail customers are using one wholesaler as their primary or main vendor," said Mel Whitmire, president of Drug Service, "and that means that since they're buying primarily from one source, they're continuing to demand additional products.

"From a wholesaler's point of view, of course, the more we can sell them, as long as we can turn it fast enough and handle it efficiently enough, the more we can grow," Whitmire added.

"When we had shorter product lines, we got less of the retailer's business," said Doug Thompson, sr. vp of distribution planning for McKesson Corp. "We prosper by expanding our product lines. We get deeper penetration into the drug stores we service."

Fuller-line companies such as McKesson and Bergen were estimating that they were now supplying 63% to 65% of an average retail customer's wholesaler needs, as opposed to less than 50% four or five years ago.

Home health looks promising

Home health care, because of the general aging of the population and because more hospitals are discharging patients earlier today to improve their own cost efficiencies, was regarded by nearly every wholesaler as a particularly promising potential new market.

Top 20 drug wholesalers

	Fiscal year ending	Estimated current year sales from drug wholesaling	% change over last year	% of total company sales generated by wholesale division
1. McKesson Drug & Health Care, San Francisco	3/31/85	$2.7B	18%	59%
2. Bergen Brunswig, Los Angeles	8/31/84	$1.4B	21	80
3. Alco Standard, Valley Forge, Pa.	9/31/84	$850M	28	25
4. FoxMeyer, Denver	3/31/85	$800M	72	94
5. Bindley Western, Indianapolis	12/31/84	$575M	20	100
6. Harris, Solon, Ohio	4/30/85	$520M	22	100
7. Amfac Burlingame, Calif.	12/31/84	$492M	10	22
8. Spectro, Jenkington, Pa.	3/27/85	$450M	15	95
9. McPike, Kansas City, Mo.	4/30/85	$349M	15	100
10. Owens & Minor, Richmond	12/31/84	$300M	18	97
11. Drug Services**, Fresno, Calif.	6/30/85	$280M	18	72
12. Ketchum, Newington, Conn.	4/30/85	$267M	15	95
13. Kauffman-Lattimer, Columbus, Ohio	9/30/84	$250M	19	100
14. Humiston-Keeling, Chicago	4/30/85	$220M	12	100
15. Durr Fillauer, Montgomery, Ala.	12/31/84	$210M	20	58
16. Southwestern, Dallas	12/31/84	$200M	18	100
17. S-P Drugs, Brooklyn, N.Y.	4/30/85	$160M	15	100
18. LAD, Rosemead, Calif.	12/31/84	$151M	16	80
19. *Cardinal Drug Distribution, Columbus, Ohio	3/31/85	$150M	291	43
20. Northwestern, Auborn, Wash.	1/31/85	$150M	20	100

Source: *Drug Store News* Wholesaler Sales Survey

*Cardinal owns Baily Drug & Ellicott Drug
**Acquired by Bergen Brunswig

***Drug Store News'* first Wholesaler Trends Survey was done in the late summer and fall of this year with the assistance of the National Wholesale Druggists' Association (NWDA).**

The survey was sent to the corporate headquarters of 107 companies operating a total of 321 distribution facilities.

The companies we surveyed generated more than $10.3 billion in sales in 1983, approximately 90% of total sales for the wholesale drug industry.

Response rate for the survey exceeded 19% and included companies operating as few as one, to as many as 50 distribution centers.

Joe Polastri, general manager of McKesson's Drug Services, was developing a new program for McKesson customers in the belief that home health care sales are going to continue to go "straight up." McKesson, like Drug Service, was using the resources of one of its divisions, the Sun Mark Home Health Care Company, to support and enrich its developing home health care program.

Drug Service was planning to use the sources and contacts developed by its sister division, Hospital Services and Supplies, to strengthen its particular home health care program.

"This is a very large potential market," said Whitmire, "and it's going to grow rapidly."

Tom Coulbourn, executive vp of Owens & Minor, called home health care "one of the most significant areas of opportunity for the retail druggist to come along in years." John Wilcox, director of sales and marketing for McPike, said the growth prospects were "phenomenal."

"In the past year, we have more than tripled our sales in this category," he said.

Entwined with the enthusiasm for home health care lines was a comparable enthusiasm for hospital accounts, seen by most wholesalers as an area for strong and dramatic sales gains.

Some wholesalers such as Owens & Minor and Drug Service were already generating a substantial percentage of total sales (45% and 50%, respectively) through hospitals, while others such as McKesson were experiencing growth rates in excess of 30%. For fiscal 1985, approximately 12% of McKesson's total sales for its wholesale division is expected to come from hospitals.

In contrast, most wholesalers reported that their growth rate among independent retailers, traditionally the wholesaler's strongest customer base, were flat or up only slightly.

Chains, surprisingly enough, were also considered a growth area for many wholesalers, and not just for those located on the West Coast. Because the wholesale industry in the past 10 years has consistently been able to lower operating expenses, pricing has become more and more competitive.

"Chains are finding that in many cases they can acquire products more efficiently from us than they can buying it direct," said a source from Bergen.

Hospital share targeted

Hospitals were also learning that same lesson. Emil Martini Jr., chairman and ceo of Bergen, estimated that within five years the wholesale industry will have a higher share of the hospital markets sales than they have today from retail drug stores.

"The hospitals are learning," said Martini, "that most wholesalers can supply them cheaper than if they buy direct. Plus, wholesalers can help keep their costs down by keeping their inventories down. And if they buy from a primary wholesaler, they deal with one invoice and one delivery. If they buy direct, they're dealing with dozens of invoices and deliveries. The cost savings are substantial."

Much of the dollar growth that the wholesale drug industry has been able to generate in the past few years has resulted from operating efficiencies that have reduced margins and made the wholesalers more price-competitive.

To some wholesalers and to some analysts on Wall Street, the decline in profit margins (down to 9.77 on average in 1983 compared with 10.48 last year and 11.63 in 1978) is serious, portending a worrisome return to the dog-eat-dog days that threatened to destroy the industry in the early to mid-70's.

But to the bigger and more progressive companies that have been able to reduce margins and lower prices through operating improvements, the trend was not frightening, but promising.

They agreed with National Wholesale Druggists' Association president Bill Ford, who pointed out that the decline in margins is offset "by an almost parallel reduction in operating expenses."

Operating expenses to net sales, Ford said, were down 7% to 7.21% in 1983 while operating expenses to gross profits were down nearly 8% to 73.82%.

"Very strong year"

Ford called 1983, a year in which the wholesale industry generated a 17% increase in sales to nearly $12 billion, "a very strong year for drug wholesalers." He said NWDA's findings indicate that the industry is continuing "to move ahead aggressively in such areas as sales growth, expense reduction, average line extensions, inventory and total asset turns and receivables."

"What you're seeing today is what I call 'value-pricing,' " said Whitmire of Drug Service. "Wholesalers may be cutting their prices but when they do they compensate by reducing collection periods."

In fact, NWDA's latest operations surveys show that the average collection period for a wholesaler today is 26.44 days, compared with 28.42 days in 1982 and 37.03 days in 1975.

The NWDA survey also shows that wholesalers are doing an excellent job on other significant profit indicators including: return on total assets, average line extensions, inventory turns, reduction of operating expenses as a percentage of both gross profits and net sales, net profit percentages and return on net worth.

"Our volume is going up and our costs of handling are going down," said Bill Williamson, chairman and ceo of Durr-Fillauer, "and that makes us the most cost-effective distribution industry in America."

Automation continues

To continue to fuel that trend, most wholesalers in 1984 were continuing to automate, upgrade or expand existing distribution facilities.

McKesson, Southwestern Drug and others were continuing to consolidate by closing older and smaller facilities while replacing them with larger ones capable of handling higher volumes and operating more efficiently. In eight years, McKesson has gone from more than 90 facilities to 50, while Southwestern has gone from 11 to four d.c.'s.

The higher-volume facilities are also being automated; automation sortation systems are being added, more programs are being computerized, scanners are being installed into higher volume d.c.'s to route orders, and at least one wholesaler, Bergen Brunswig, is testing automatic single-item picking machines in one of its highest-volume d.c.'s—while Southwestern is preparing to go on line with a "state of the art" perpetual inventory automatic replenishment system.

"For productivity enhancements,"

Continued on page 21

Number of wholesaler distribution centers in operation

Company	1984	1983
McKesson Drug	49	50
Amfac Drug	41	42
Bergen Brunswig	29	29
Owens Minor	23	20
FoxMeyer	15	11
Drug Services	10	9
Bindley Western	6	6
Harris Wholesalers	6	5
Durr Fillauer	5	5
Spectro	5	5
Humiston-Keeling	4	4
Kauffman-Lattimer	4	4
Southwestern Drug	4	4
LAD Drug	4	4
Ketchum Distributors	4	4
Cardinal Distributors	4	1

1984 Annual Report of the Wholesale Drug Industry

Drug wholesaling sales may reach $14 billion

Continued from page 17

says Steve Westall, senior vice president of LAD Drug, "we are shrinking the size of the areas we work in, picking more efficiently, computerizing stock replenishments, computerizing sortation systems, conveyor systems, etc.

"Even though all of our d.c.'s except one are unionized, we've still managed to reduce operating expenses as a percentage of sales from a high of 8% a few years ago to 5% today."

A few wholesalers think the industry today may have gone about as far as it's able to go in reducing operating expenses, but Westall disagrees.

"I think the wholesale industry is going to continue to grow like this. The companies in this industry have always been innovative. Look at order/entry. In a short while, you're going to see a great surge in automatic order replenishments and that will lead to additional cost savings."

"Value added services"

And, in what promises to be an increasing boon to retailers, as wholesalers save money, they are plowing more of it into marketing programs in the form of what is now popularly known as "value added services."

This means the typical drug store retailer, whether chain or independent, can increasingly turn to his or her wholesaler for help with inventory management, planograms, pricing, financial services, promotional assistance, accounting, etc.

Drug Service, for instance, has a new automatic in-store accounts-receivable program that permits a retailer to automatically transmit accounts receivables to wholesaler headquarters. Drug Service, in turn, prepares the statements for its customers.

McKesson has a number of customer-service programs including a rapidly growing service merchandise program called Cos Mck; Bergen has a space management program, plus a number of promotional programs in additional to the traditional merchandising and pricing programs that most of the major wholesalers offer; FoxMeyer has a broad range of promotional programs, etc.

"Service orientation is a trend now," said Chester Milligan, president of Amfac Distribution and Health Care. "McKesson and Bergen have done an excellent job of molding the industry toward a marketing concept that stresses service. It really started with the shift to automated order/entry systems. Out of that came velocity reports, inventory management reports, planogramming, the whole marketing/merchandising value added services concept."

"For the past 10 years, the industry has been moving toward a service distinction, not just a price distinction," said Doug Thompson, McKesson's senior vp of Distribution Planning. "A service distinction makes it possible for a wholesalee to stand out from his competition. Plus it makes it easier for the more cost-efficient companies to compete. They're able to attract customers from those companies that are not as efficient."

Co-op advertising expanding

The thrust of competition is also creating another trend that is benefiting independent retailers: the creation and expansion of voluntary or cooperative advertising programs.

McKesson has the largest and perhaps oldest voluntary group, the 1,600-member Valu-Rite based in Los Angeles, but Bergen Brunswig has a growing voluntary association called Good Neighbor. FoxMeyer has its thriving Health Mart, Durr-Fillauer has Price Guard, Drug Service has Prime Value, Owens & Minor has Cardinal Drug, Dik Drug has Centsible, etc.

Many of these groups are less than a few years old, but all seem to be growing.

"There will have to be more action with voluntaries," said Rex Molson, president of McKesson's Drug and Health Care Division. "Independents need to belong to something so that over the long run, they can get the advantages and economies of scale. That's the only way they're going to be able to compete with chains."

Bergen, whose staff for its Good Neighbor program were recruited directly from the retail side of the business, is investing about $500,000 a year in advertising revenues for the program and hopes to use Good Neighbor to create a strong identity for its approximately 500 members.

In certain pockets such as Fresno, Calif., where the program has been in place for over a year, vp of merchandising Tom Allison reports "a growing awareness on the part of the consumer to the Good Neighbor names and services."

"All voluntaries," said Ron Bone, president of McKesson's Valu-Rite, "try to provide independents with the promotional tools that will make them more successful. The idea is to provide them with a way to keep their autonomy, but at the same time take advantage of the kinds of purchasing and distributional and promotional economies a chain can enjoy."

Sales pace expected to continue into 1985

The wholesale drug industry increased sales 17% in 1983 to $11.9 billion.

According to the most recent National Wholesale Druggists' Association's Operating Survey, about 10 points of that total growth is "real," or minus inflation. The NWDA inflation index, which measures increases in product prices, rose only 7% in 1983.

If the industry simply maintains that same rate of growth for 1984, as it seems to be doing, total wholesale drug sales will come close to and possibly exceed $14 billion.

To date most of the major companies, such as McKesson, Bergen, ALCO and FoxMeyer, are already ahead of that growth, with sales increases generally averaging more than 20%.

Many of the midsize to smaller companies, however, are generating sales increases in the 12% to 20% range.

The industry suffered some criticism in 1983 for alleged "profitability slippage," but that slippage was mostly tied to a decline in the average profit margin for the industry. Those who criticized the trend failed to take into account offsetting factors such as substantial declines in average operating expenses with simultaneous increases in average volume sales.

"NWDA's numbers show that there's a decline in net profit from 1.41% in 1982 to 1.37% in 1983," said Joel Liffman, an analyst for Drexel Burham, "but I don't consider that a meaningful number.

"If you round off the number, there is really a zero change. Much more meaningful is the fact that as a general trend, gross profitability in the industry is increasing.

"Operating expenses are not growing as fast as sales. Revenues in this industry are growing quicker than expenses, which means that this industry is fairly well leveraged."

Bill Ford, president of NWDA, points out that the ratio of net sales to total assets in 1983 hit "an all-time high" while average annual inventory rates increased substantially and the average collection period in days went down dramatically.

The result was that net profits after taxes declined slightly in 1983, down from an all-time high of 15.55% in 1982 to 15.23% in 1983. Ford said the 15.23% return was a "very strong showing."

"Some people say the wholesale industry has already done so much to improve profitability by reducing expenses and improving productivity that there's very little room for any further growth, but I don't agree with that," said Gene Vykukal, president of Southwestern Drug.

Trends in customer sales mix for the wholesale drug industry (percentage of gross sales)

	1977	1978	1979	1980	1981	1982	1983
Independent drug stores	63%	62%	61%	59%	57%	56%	55%
Chain drug stores	22	21	21	22	23	22	21
Hospitals	10	11	11	12	14	16	17
Chain drug warehouses	3	4	5	4	3	3	4
Clinics, nursing homes, & others	1	2	2	2	2	2	2
Food & mass merchandise stores	1	2	2	2	2	2	2

Source: NWDA survey

"There's going to be increased profitability as individual distribution centers continue to generate higher volumes and as further technological innovations like automatic replenishment find their way into more facilities."

"We're going to be able to improve our operating efficiencies," said Doug Thompson, senior vp of distribution planning for McKesson, "because we're consolidating our warehouses and generating larger concentrations of volume out of individual facilities.

Thompson also said the company had made gains in productivity because of new software for distribution efficiencies.

"Once we have perpetual inventories and automatic replenishment," said Vykukal, "you are going to see an even more dramatic improvement in turns. Plus wholesalers will be able to invest their money where it should be invested: in products that turn."

Southwestern will be implementing a perpetual inventory/automatic replenishment system in the spring of next year, probably by April, Vykukal estimated.

John Gilbert Smith, the president of Ketchum, believes that the drug industry at both the retail and wholesale level is "very viable. Our growth and the ser-

Continued on page 24

Key operating statistics for the wholesale drug industry*

Year	Gross profit %	Operating expense %	Operating profit %	Net profit %	Return on net worth
1980	11.15	8.53	2.62	1.32	12.72
1981	11.07	8.30	2.74	1.35	13.60
1982	10.48	7.79	2.68	1.41	15.55
1983	9.77	7.21	2.56	1.37	15.23
1984 Est.	10.4	7.1	3.3	1.6	17.0

Source: NWDA survey & Drexel Burnham Lambert estimates
*LIFO estimates

Breakout of wholesaler sales by product mix

	1983 Wholesale drug industry sales (billions)	% of net sales
Pharmaceuticals	$ 8.11	68%
Proprietary	1.78	15
Toiletry	1.09	9
Sundry	0.74	6
Other	0.18	2
Total	11.90	100

Source: NWDA survey

1984 Annual Report of the Wholesale Drug Industry

Sales pace expected to continue into 1985

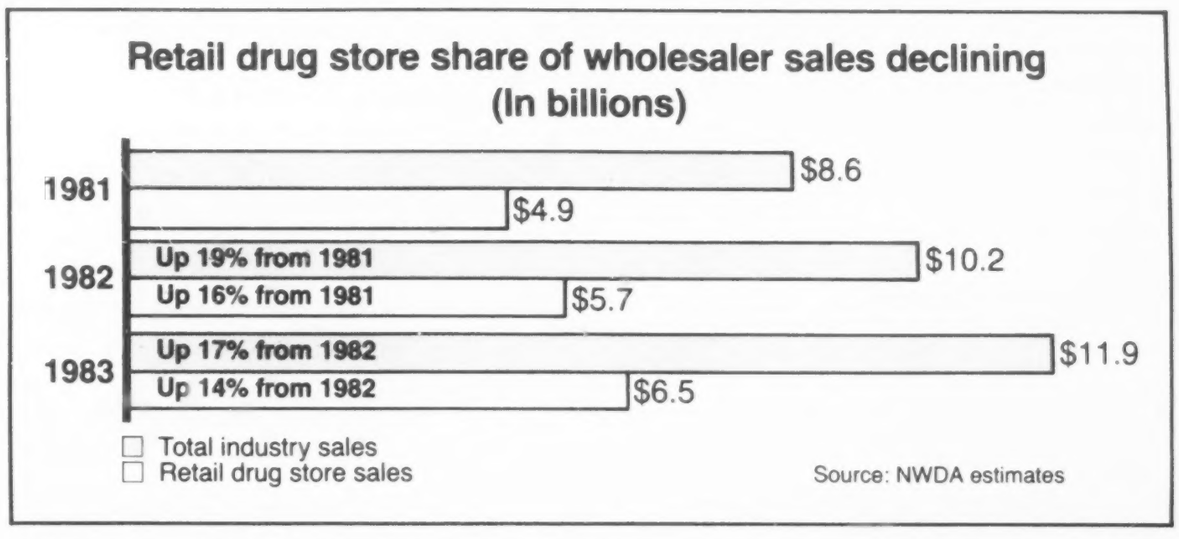
Continued from page 21

vices we render," he said, "are only limited by our imagination."

Most wholesalers are aggressively pursuing volume growth from a variety of strategies. They range from acquisitions through the consolidation of distribution facilities through the search for new customer markets: hospitals, HMO's, nursing homes, veterinarian services, department stores, food stores, etc., as well as through the addition of new lines that enable the distributor to provide individual customers with greater varieties of products: home health care items, medical surgical supplies, sports medicine, school supplies, stationery, pet care, fragrances, cosmetics, hair care accessories, etc.

Wholesalers are also continuing to capture an ever-increasing share of the United States pharmaceutical business. According to the most recent study done by the Pharmaceutical Manufacturers Association, wholesalers have increased their share of total pharmaceutical sales to 60% in 1980 from just 48.5% in 1976.

Emil Martini Jr., chairman and ceo of Bergen Brunswig, estimated that by 1985 the industry will capture "at least a 65% share and that could conceivably be much higher."



"Customers," Martini said, "seem to be accelerating the rate at which they are purchasing pharmaceuticals from distributors." He attributes this to operating efficiencies such as electronic order-entry, productivity enhancements, etc., that enable the majority of wholesalers "to reduce our operating expenses and pass the savings on to make our pricing more competitive."

Martini also noted that the near future will bring improved delivery systems and many new pharmaceutical products—such as transdermal patches—that will be relatively higher-priced. "Most of these higher-priced [and therefore more profitable] items," he says, "will be distributed through wholesalers."

Bill Williamson, chairman of Durr-Fillauer, put the point in succinct terms when he said, "The industry's volume is going up and our costs of handling merchandise are going down. Ours is the most cost-effective distribution industry in America."

Trends in the average wholesaler's product mix (% of net sales)

	1979	1980	1981	1982	1983
Pharmaceuticals	63.4%	63.6%	64.7%	65.3%	68.2%
Proprietary	17.3	17.3	17.6	15.6	14.5
Toiletry	9.7	10.7	9.3	9.5	9.1
Sundry	8.3	7.0	6.8	7.9	6.3
Other	1.3	1.4	1.6	1.7	1.5

Source: NWDA survey

Wholesalers anticipate growing hospital sales

For the past two years, hospitals have been the strongest growth areas for wholesalers, with most industry members projecting that the trend will continue strongly for the next two years.

According to *Drug Store News*' first Wholesaler Trends Study, nearly 9 out of every 10 wholesaling companies have experienced sales increases in hospital business for the past two years while 80% of all wholesalers believe this growth will continue at least for the next two years.

According to the survey, many wholesalers have increased their hospital sales between 30% and 50% in the past year alone.

More than 60% of the companies who responded to our survey were doing more than 20% of their total business with hospitals, while several of our respondents had total sales in excess of 40% and 50%.

Only 1 out of every 10 respondents believed their sales to hospitals might decrease in the coming two years, while 8 out of 10 believed their sales would go up dramatically.

Many respondents (70%) also reported dramatic increases in sales direct to chain drug stores, while a smaller number, 20%, also reported that at the same time sales to chain warehouses had also gone up considerably over the past two years.

More than 80% of our respondents felt that sales direct to chain stores will continue to increase in the future, while 4 out of 10 felt this pattern would continue with respect to chain warehouses.

The current percentage of sales direct to a chain store ranged from a low of 2% to a high of 30% for respondents selling to this marketplace. Most respondents were doing only between 1% and 10% of their business with chain warehouses, but there were exceptions: one respondent was currently doing more than 80% of its business with chain warehouses.

The prime customer for most of our wholesaler respondents was still the independent community retailer. More than 80% of our respondents reported that business with independents had increased in the past two years, while 80% also felt it would continue to increase.

In addition to hospitals, the most promising areas for future new sales growth were the following: independents, chain stores direct, chain warehouses, nursing home suppliers, nursing homes direct, food stores, mass merchandise stores, convalescent aids stores, HMO's and clinics.

Some respondents were currently generating as much as 28% of their total sales through mass merchandisers, but the average ranged from 2% to 4%. For most respondents, sales to HMO's and clinics ranged from a low of 1% to a high of 5%, while sales to nursing home suppliers, for those in this business, ranged from 3% to 5%. Sales to nursing homes direct hovered between 1% and 3%, but some respondents reported they would not pursue this line of business because it would put them in competition with retail customers.

For those respondents doing business with food stores, the per cent of total sales ranged from 1% to 3%.

Over the course of the next two years, however, nearly 45% of our respondents felt that sales to nursing home suppliers would increase while 15% believed this would also happen with food stores.

Five out of 10 of our respondents also felt sales to clinics and HMO's would go up in the next two years, while 20% believed the same would happen with mass merchandise stores.

Despite the fact that only one wholesaler was currently selling direct to physicians, 15% of our respondents felt this market would grow.

More than half the respondents in our survey supported a voluntary or a more limited form of promotional advertising program. The percentage of total wholesaler sales generated by these various memberships varied widely, ranging from a low of 0.03% of sales to a high of 15% of sales. The average, however, was around 12%.

In marketing services, just about every respondent featured a broad assortment of merchandising support programs such as planograms, point-of-purchase and point-of-sale aids, etc. Nearly everyone also had promotional programs such as price update reports and customized price labels based on the gross margins desired by retailers.

More than 80% of our respondents also provided retail customers with help with store fixtures, while 75% had store-remodeling programs, and 65% had host support for computer programs. More than 80% of our respondents provided their customers with both hardware and software for in-store pharmacy computer programs while another 65% had some form of financial assistance programs available.

Another 10% were also adding site selection assistance to their marketing programs while over 50% already had such a service. Nearly 9 out of 10 respondents also offered product-movement reports while 85% provided inventory control reports and pharmaceutical generics program. Just 40%, however, had private-label programs, while only 30% had management reports. Only 5% offered business insurance.

Some 25% of our respondents, however, were planning to add business insurance and financial/management report programs (profit and loss reports, labor scheduling reports, etc.) to their stable of marketing services, while another 15% were planning to add private-label.

Ten per cent were also planning to add site selection assistance and in-store computer host support.

Most of our wholesaler respondents were also giving their retailers help in developing a zone-pricing program. Nearly 9 out of every 10 wholesalers had such a service available for H&BA and OTC products, while 50% also offered it for pharmaceutical products.

In the area of product mix, all of our respondents were generating the bulk of their sales from pharmaceuticals. Pharmaceuticals as a percentage of sales ranged from a low of 60% for the most diversified full-line companies to a high of 90% for those houses that were primarily pharmaceutical suppliers.

All our respondents had at least some selection of H&BA and OTC products available.

Many respondents did not specify whether they included such lines as candy, gifts, personal appliances, toys, etc. in either sundries and seasonals.

Growth patterns in the average wholesaler's customer mix

	Sales rose in past two years	Expect sales rise in next two years
Hospitals	87%	80%
Independents	80	80
Chains direct	70	80
Home health care and convalescent aid stores	40	25
Mass merchandise stores	15	20
Clinics and HMO's	30	50
Nursing homes direct	25	25
Nursing home suppliers	25	45
Chain warehouses	20	40
Food stores	20	15
Physicians	5	15

Source: *Drug Store News* 1984 Wholesaler Trends Study

1984 Annual Report of the Wholesale Drug Industry

Service translates into growth at McKesson

SAN FRANCISCO — McKesson Drug & Health Care, the largest division of the McKesson Corporation and the nation's No. 1 drug wholesaler, is continuing to court growth by putting its marketing emphasis on service.

The group, which was the first to coin the term "value-added services" now used by the entire drug-wholesaling industry, has just developed a new financial and business study package for its retail customers.

McKesson

The study package, which McKesson plans to make available to any interested retailer, consists of a series of seven modules built around video cassettes addressing specific problems.

"It's like a Harvard case history," says Joe Polastri, a group executive vp and general manager of the drug company. "We taped a retailer trying to cope with a specific problem. It might be cash management or inventory control or gross-margin analysis. We're showing those tapes at seminars that we've set up in various sections of the country. Our merchandising reps lead the seminars and they try to help retailers figure out the best strategies to adopt given the nature of that particular problem."

Both Polastri and Rex Malson, president of the Drug & Health Care Group and a corporation vp, feel that the era of chains madly gobbling up market share at the expense of independents is ending, but that independents still need to improve their business and financial skills if they are going to prosper.

"The weak," says Polastri, "have already been weeded out by the chains. But there are still lots of retailers out there having a tough time, and this kind of program is designed to help them."

McKesson is also continuing to expand its Cos Mck service merchandising program. For an agreed upon fee, a McKesson rep will set, stock, replenish, price label and maintain just about any department in a retail drug store. The most commonly repped departments, however, are cosmetics, costume jewelry, hosiery, pet care, stationery and fragrances.

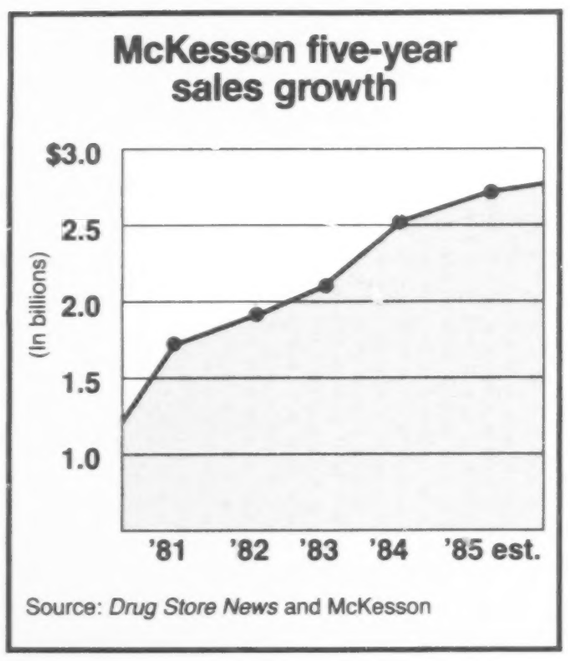
"The service levels we provide are a way to distinguish ourselves from our competition," says Doug Thompson, McKesson's senior vp of distribution planning.

"For the past 10 years, this industry has been moving toward service distinctions rather than just price distinctions. Price competition is still a logical and plausible business strategy, but it doesn't take a genius to figure out how to give away profit. As an industry, we've been in that loop for a long, long time."

Like its closest competitor, Bergen Brunswig, McKesson has been aggressively moving to automate its operations and expand into new customer areas.

The chain's newest warehouse in Sacramento has an automated sortation system as well as a picking system sequenced by "families" of traditional drug store departments. All dental care products, for instance, are in the dental care "department" of the warehouse and each incoming order from a retailer is presorted by computer so that pickers can fill all dental product orders at one time.

To get even more productivity out of its distribution centers, McKesson is also putting in mezzanines that allow pickers to work from storage space that was previously just "empty air." The cube in a McKesson warehouse is now averaging 30 ft. instead of 24 ft. "It's just more efficient to stack higher," says Polastri.



Because of its operational efficiencies, Sacramento is now McKesson's most active facility. In mid 1984, it was running at 1987 sales projections and with a capacity of a million lines a month, handling close to 750,000.

Consolidated centers

For the past eight years, McKesson has been consolidating its warehouses, closing smaller facilities and replacing them with much larger more centralized facilities like the one in Sacramento.

The move from smaller to larger, according to Polastri and Thompson, permits each facility to stock from between 1,000 to 1,500 more items, enabling McKesson, in Thompson's words, "to improve customer service."

"Even though our consolidated centers may be further from the customer service point," says Thompson, "they usually have larger inventories and that means that our retail customers now have many more unique items available to them."

The move, of course, also enables McKesson to improve its operational efficiencies because each consolidated center handles larger volumes of business.

Thompson points out that McKesson is more than 50% ahead of the industry's median average on office productivity (number of order lines processed per man-hour) and 80% ahead on warehouse productivity (number of lines picked per man-hour).

More products

The centers are also continuing to carry more and more diversified products. In addition to pharmaceuticals, H&BA and OTC products, McKesson now stocks a full line of stationery and school and office supplies, pet supplies, reading glasses, hair notions and fragrances (also available through McKesson's Fragrance Division, one of nine subdivisions now grouped into the Drug & Health Care Division).

"We are carrying more products that go into the center of the store," says Polastri. "And we're also filling in more products for the perimeters of the store. We feel the more orders we can fill, the more we can grow."

McKesson's management feels independents, chains and hospitals will be the strongest avenues for future growth, but the company is also continuing to supply product to food stores and mass merchandisers and there is a chance McKesson may form a service merchandise division to help food stores market H&BA and OTC products.

"The hospital business is growing by leaps and bounds," says Polastri. "We were up 35% in sales last year and so far, this year, we're up 32%."

Like most wholesalers, McKesson is trying to position itself as a "prime vendor" for both its retail and hospital customers. So far, the concept is working. McKesson's management estimates that the company is a prime vendor (the No. 1 source of supply for an individual account) to at least 80% of its drug store retail customers.

Wholesaler Profiles

Bergen sees boom sparked by electronics

LOS ANGELES — Bergen Brunswig, the wholesaler with the second-highest volume in the country, is projecting a growth rate of between 20% to 25% annually for the next five years.

Bergen's chairman and ceo Emil Martini estimates that the company's most dramatic growth will come from its consumer electronic division. Sales for the division for the past 10 years have already increased 10-fold.

However, in the drug distribution

Bergen Brunswig Corporation

arena, growth is expected to come from two key areas: an expanded customer base and an extended product mix.

Bergen's vice president of merchandising Tom Allison estimates that the company's nearly two-year-old voluntary, the Good Neighbor program, will have about 500 members by the end of 1984. "We're growing at a rate of about 20% a year," Allison said.

Like many wholesalers, Bergen is also aggressively going after more hospital business as well as "aggressively pursuing," in Martini's words, more sales to HMO's.

"Over the long term, we expect to have a higher share of hospital business than retail business," said Martini. "Hospitals are where retail drug stores were about 10 years ago. They are just starting to discover the economic benefits of a prime-vendor supplier."

Seven years ago, hospitals only accounted for about 6% of Bergen's total customers. Today, they account for 26%. Chains are also a source of growth for the company. In 1977, chains only accounted for about 24% of Bergen's overall business. Today, they account for about 33%.

But with more than 4,200 independent retail accounts currently being serviced, independents are still the heart of Bergen's business. Last year, they accounted for 47% of the drug company's total sales.

Bergen has been trying to nurture this side of its business by developing a wide variety of retailing and merchandising support programs, such as Bergen's space management program, to which about 60% of its retail accounts belong, and a Super Saver program that Allison believes helps independents add a "bargain atmosphere" to their stores.

Bergen's space management program is a planograming support and merchandising system, while Space Saver is more promotional.

About 80% of Bergen's retail customers belong to Super Saver. For a membership fee, participants get complete in-store monthly promotional packages, which usually feature eight to 10 spotlighted, high-velocity products that change every other week.

With the package comes color coordinated signs that, when hung within a store, create a "carnival atmosphere." Also shelf talkers, window signs, hand bills, and a black and white velox for ads are offered. Bergen supports the program with spot TV as well as radio and print ads.

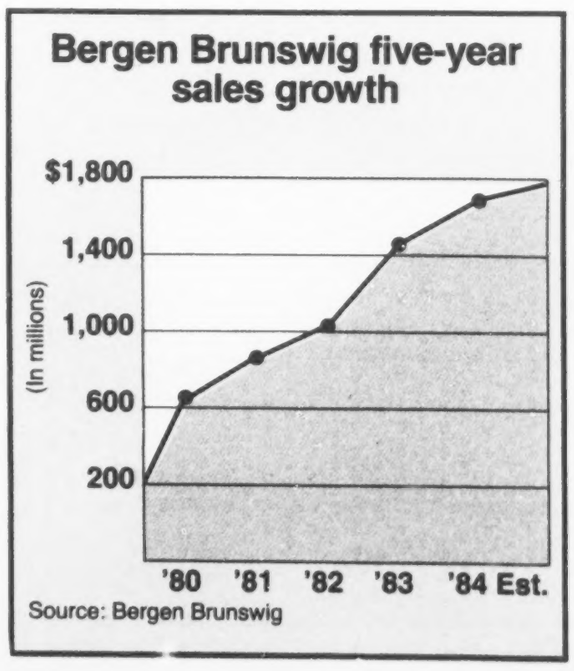
In the area of line extensions, Bergen is currently working on the development of a new home health care program while simultaneously rolling out a new line of about 1,000 stationery sku's.

"Sundries and stationery are getting a lot of attention from us," Allison said. "We'll be expanding even more next year." Through its new line of consumer products, Bergen is already distributing pantyhose, watches, batteries and baby care. It is considering adding more seasonal items such as lawn chairs and barbecue grills.

Earlier this year, Bergen began testing an automatic picking machine in its San Jose, Calif., warehouse. Martini said the $750,000 system will probably pay for itself within three and a half years.

He said similar computerized systems will probably be added to other Bergen distribution centers "wherever the volume of pharmaceutical business justifies their investments."

Of Bergen's 50 distribution facilities, 29 are currently used for drug wholesaling. The Drug Wholesale Group accounted for about 80% of the company's total sales last year.



1984 Annual Report of the Wholesale Drug Industry

Wholesaler Profiles

Acquisitions push Alco Health into third place

VALLEY FORGE, Pa. — With its voracious appetite for acquisitions and its keen ability to tune into thriving trends, Alco Health Services has become the third-largest full-service pharmaceutical distributor in the country within a span of only six years.

Alco Health Services is the drug wholesaling arm of Alco Standard, a huge conglomerate that posted 1983 earnings of $57.2 million on sales of $2.8 billion. During 1983, Alco Standard shed several of its manufacturing operations in order to concentrate on its thriving distribution properties, including Health Services. In fact, Alco Health Services, which posted a 19% increase in 1983 sales for a total of $691.3 million is the company's fastest-growing segment and second largest behind its paper division.

Alco Standard's president and ceo, Ray B. Mundt, sees big things ahead for full-service pharmaceutical distributing. In fact, he said that as new drugs hit the market and manufacturers continue to sell more pharmaceuticals through wholesale channels, the market could swell to more than $14 billion by 1985. That's more than double its size four years ago. For Alco, the Health Services division is attractive because of a 25% return on capital.

Acquisitions have played a key role in Alco Health Services growth. When the company "acquires" another, it actually merges all operations (including personnel) into its corporate umbrella. According to the company, this encourages an entrepreneurial spirit within the company.

One of the most recent acquisitions was that of Brown Drug, which serves stores in Sioux Fall, S.D., Council Bluffs, Iowa and Makato, Minn. With the addition of Brown, Alco thrust itself into new markets. Its existing base includes: The Drug House Inc., Brotherston Health Care Services, Brotherston Hospital Supply, Duff Brothers Inc., The Geer Drug Company, The Kauffman-Lattimer Company, Rita-Ann Distributors, Smith-Higgins Inc., William T. Stover Company Inc., Strother Drug Company and Spetrum Corporation. The Alco Health Services serves 23 states from New York and Pennsylvania south to Georgia and west to Texas.

It is obvious that Alco Health Services' growth has not only been geographic, but into new categories, as well. Last year, for example, Alco ventured into the prestige fragrance, cosmetics and gift business with the purchase of Rita-Ann Distributors.

Additionally, Alco is entering the home health care business with its Total Home Health Care programs. Under this plan, retailers can gain access to Alco's home health care products and tap into the company's merchandising savvy.

Another important program is Alco's Family Independent Pharmacy voluntary program. The voluntary program is set up to attract small pharmacies into Alco's distribution network. It offers them advertising support, access to Alco's computers to manage inventories, planograms, traffic analysis, value-added product lines, store graphics and other managerial tools.

Purchases put FoxMeyer in new markets

DENVER — FoxMeyer began fiscal 1985 the way it closed the books on fiscal 1984—with a series of acquisitions.

In April, FoxMeyer completed the the acquisition of I. L. Lyons, the New Orleans wholesaler, which last year posted operating earnings of $1.9 million on sales of $98.3 million.

Four months later, FoxMeyer signed a letter of intent to purchase Yahr-Lange for $15.25 million in cash. The purchase of Yahr-Lange, which last year earned $2.5 million on sales of $118.6 million, opens up two more important markets to FoxMeyer. To the north, Yahr-Lange is the No. 1 wholesaler in Milwaukee and the surrounding markets. Headquartered in Elm Grove, Wis., the company also operates distribution centers in Rockford, Ill., and La Crosse, Wis. In Florida, Yahr-Lange commands the No. 2 position in many markets, with distribution centers in Miami and Lakeland, Fla. Prior to the acquisition, FoxMeyer had no facilities in Wisconsin and only a marginal presence in the Florida panhandle.

Last month, FoxMeyer struck again. This time it was the Arlington, Tex., computer services firm, PharmAssist. When the purchase is completed FoxMeyer will have doubled its base of pharmacy computer system users to nearly 2,600. PharmAssist provides computer services and products to an estimated 1,300 pharmacies in 29 states.

FoxMeyer's seemingly insatiable appetite for other wholesale operations and pharmacy computer firms has been well received on Wall Street. The wholesaler last month raised nearly $44 million in a stock offering of nearly two million shares. Proceeds from the offering were to be used to retire bank debt from previous acquisitions, the company said.

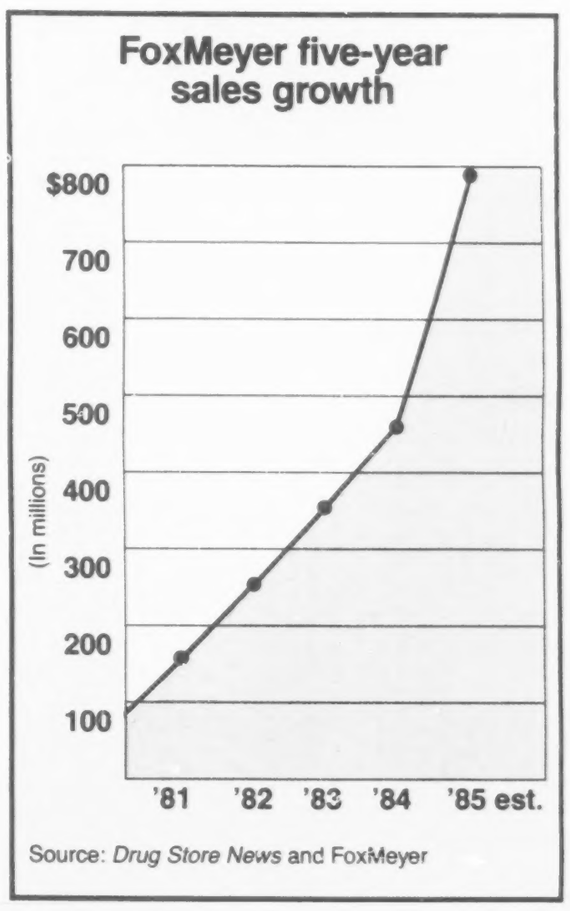
Part of the reason that FoxMeyer has had little difficulty raising capital for expansion is that the wholesaler has been able to quickly assimilate each of the acquisitions into its own operations. In addition, many analysts have been impressed with the company's outstanding financial performance.

For the fiscal year ended March 3, FoxMeyer's net income soared 126% to $5.2 million from $2.3 million earned in the previous year. Sales advanced 32% to $464 million from $351 million in fiscal 1983.

In addition, first-quarter results seem to indicate a continuation of the upward trend. Net income for the first quarter, ended June 30, jumped 102% to $1.4 million from $704,000 from the first quarter of the previous year. Sales rose 56% during the first quarter to $159.4 million from $102.3 million last year.

The pending purchase of PharmAssist ranks as one of FoxMeyer's most significant acquisitions since the company went public in 1983. It complements the wholesaler's acquisitions of TBL, the pharmacy computer product and services firm in Texas that FoxMeyer merged into its Pharm-Data computer service division almost one year ago.

FoxMeyer has exploited the pharmacy computer as a means of attracting new accounts, particularly nontraditional pharmacy retailers, better than most other wholesalers. This year for instance, FoxMeyer contracted to install more than 1,000 Pharm-Data microcomputers in K mart pharmacy stores throughout the country over the next three years. Sales to K mart, alone, represent approximately 6% of FoxMeyer's total volume. Overall, the wholesaler's business with discounters and supermarket chains such as Wal-Mart, Safeway, King Sooper and Albertson's accounts for approximately 25% of its sales.



FoxMeyer expects its business with mass merchandisers and food chains to continue to have a major impact on its bottom line.

Investments aid Bindley income spiral

INDIANAPOLIS — While other drug wholesalers made a concerted effort last year to accelerate expansion through the acquisition of smaller wholesalers, Bindley Western parked much of its internal reserves in cash and marketable securities.

The strategy has paid off handsomely for Bindley thus far. Together, earnings from the distribution of ethical pharmaceuticals and income derived from investments sent total corporate income for the first half of fiscal year 1985 skyrocketing 68% to $2.3 million from $1.4 million during the same period last year. On a per-share basis, earnings rose 16% to 72¢ from 62¢ during the first two quarters of 1983. Bindley's sales for the first half of the year were up nearly 14% to $264.9 million from $232.7 million.

Last year, Bindley raised nearly $20 million from its first stock offering. At the time, William E. Bindley, chairman and ceo of the company, indicated that the wholesaler would be looking to expand in existing markets by acquiring smaller companies. However, while acquisition opportunities presented themselves, Bindley has been very selective and instead has directed its efforts toward growing internally.

"We've looked at a number of possible acquisition targets," said Jack Laughner, president of Bindley Western Drug Co. "But we're not going to buy something just for the exercise of buying another company."

Part of the reason that Bindley has been so selective in making any acquisitions is that the wholesaler is one of a dwindling number of houses whose principal business is the distribution of ethical pharmaceuticals. Approximately 95% of Bindley's total sales are generated through the sale of pharmaceuticals.

Bindley has not ruled out purchasing a full-line wholesaler. According to Laughner, while Bindley would make some "modifications" to anything it bought, "we'd probably leave a full-line house intact."

But until Bindley makes such an acquisition, Laughner says, the company's cash position and absence of any long-term debt is a "win-win situation." At the close of fiscal 1984, Bindley had amassed nearly $25 million in cash and marketable securities. Of the $9.44 per-share in shareholders' equity, $7.53 per share represented cash and other liquid instruments. In addition, Bindley has a line of credit totaling approximately $21 million. However, Laughner said that any future acquisitions will likely be financed internally.

Bindley also has used some of its capital reserves to open a new distribution center in Dallas and relocate to a larger facility in its Phoenix operating region.

Though supermarkets and discounters represent a growing segment of Bindley's business, its principal customers remain chain drug stores. Laughner said that five chains account for about 80% of the total business Bindley does with the chain drug industry. The company's biggest customers are Eckerd Drug, Revco, Rite Aid and Hook

Bindley is able to supply West Coast chains such as Thrifty without having a distribution center closer than Phoenix because it ships full case lots directly to chain drug warehouses.

In addition to its retail customers, Bindley like other wholesalers, has seen its hospital supply business increase sharply. "No question about it," says Laughner, "this will be a big part of the wholesale business." Bindley's sales to hospitals, while accounting for only 5% to 6% of total volume, have doubled in the past year.

1984 Annual Report of the Wholesale Drug Industry

Amfac focus the same despite name change

BURLINGAME, Calif. — The name has been changed from Amfac Drug Supply to Amfac Health Care, but the primary focus remains the same: doing better at what it does best. That is, supplying pharmaceuticals and OTC to drug stores and hospitals as a secondary-source wholesaler.

Even so, the Health Care Division is keeping its options open. The tip-off is the name-change. Says Chester Milligan, president of the Health Care Division: "The name Drug Supply, which implies drugs for humans only, no longer reflects our current or future plans because of our acquisition of two veterinary supply companies last June. Also, we intend to get into other health-care related areas—probably by acquisition on a selective basis." Milligan declines to be more specific at this time.

The Health Care Division prides itself on being a lean-and-mean operation. The pay-off? "Our return on investment is among the best in the industry," says Milligan.

Currently, the Health Care Division is trying to maximize its strengths in retail/hospital services in order to fill what Amfac perceives as a widening vacuum.

The vacuum is due to full-line wholesalers reducing frequency of deliveries, and to a large extent, dictating delivery days. In addition, full-line wholesalers are setting minimum orders that impede the flexibility of retailers.

Milligan says his division is keying its growth expectations on two product areas—pharmaceuticals/OTC and veterinary supplies—and two market areas—chains and hospitals.

Pharmaceuticals and OTC. He projects a 20% increase in product lines for both. He also says the company is planning to open new branches in the Northeast and Southeast, both by acquisition and start-ups.

Veterinary. This represents a quantum leap for Amfac. Why veterinary? "It is a totally different business than our traditional pharmaceutical wholesaling role. It is a sales representative-intensive business rather than product-oriented. So expenses are high—but so are sales and gross margins."

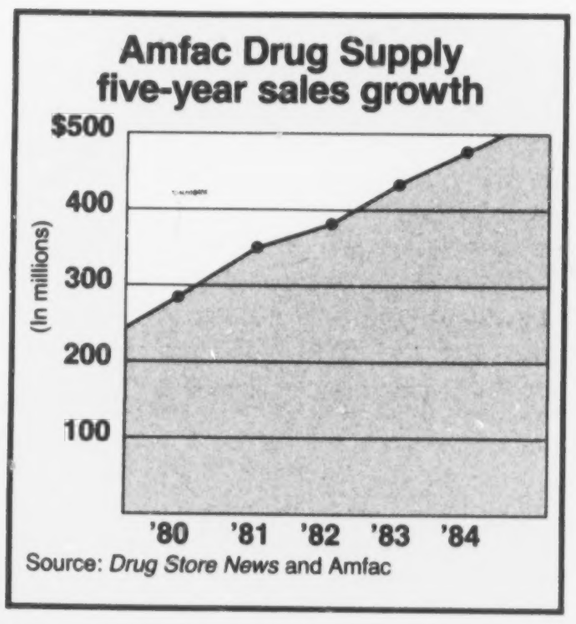
The acquisition of Holmes Serum Co., and Connrex-Mosher Veterinary Services Co., provided a distribution base in 15 states.

Veterinary pharmaceuticals represent a $2.4 billion market in the United States, and the wholesaler's share is $1 billion. The market is expected to grow 12% to 15% a year over the next five years.

Chains According to Milligan, "independents own 60% of the retail drug business. The growth is in the chains. In the last few years our sales to chains has been increasing 16% annually, and I think this trend will continue." At present, Amfac services 12,000 independents and 3.000 chain stores.

Hospitals. Growth has been about 20% a year. "Hospitals, as well as chain drug stores, need the availability of frequent deliveries not only to prevent inventory shortages but also to allow flexibility and operational efficiency derived by utilizing wholesaler inventory rather than investing their own dollars. We are uniquely qualified to provide service to these markets."

Wholesaler Profiles



Asked about venturing into the general merchandise area, Milligan said: "If we do it, it will be as a sister-business, not part of drug. Gm requires different expertise, management and handling systems. At present our branch offices are not geared for it."

Amfac operates four regional offices: Los Angeles, Seattle, Dallas and Indianapolis.

The Health care division now has 41 distribution centers and services 39 states. The centers stock 10,000 to 11,000 sku's and plan to increase that number 20%. The centers are now being upgraded for computerized support systems, beginning with electronic order entry.

Amfac's Distribution Group is one of five groups in Amfac's corporate lineup, which includes retail, hotel/resort, food and Hawaiian sugar and land. The Distribution Group accounts for approximately half of the corporation's $2.4 billion volume.

Sales climb 16% at Spectro Industries

JENKINTOWN, Pa. — Spectro Industries is celebrating its 16th year of steadily rising sales, crediting much of its success to its constantly expanding home health care and pharmaceutical lines for the growing number of elderly.

It's no wonder that Spectro, based in Jenkintown, Pa., has adopted an unequivocal corporate objective to concentrate on the burgeoning health care industry and is currently developing and distributing new products in this field.

However, Spectro, which calls itself The Healthcare Company, is not limiting its growth to this market. In the past year, it purchased Harry Toub & Sons Inc., a New Jersey-based distributor of stationery, school supplies and notions. The new division, Toub Distributors Inc., provides planogramming, promotional and regular merchandise to all of Spectro's distribution areas.

During fiscal 1984, which ended in March, Spectro recorded sales of $395.4 million, a 16% increase from the previous year's $33.9 million. Sales in 1985 are expected to increase 15%, to about $450 million.

Net income reached a record level of more than $7.2 million, a 34% increase from the $5.4 million earned the previous year. This is Spectro's third year of annual income increases of more than 27%.

Spectro is divided into a manufacturing and a distribution division, the latter accounting for 95% of the company's sales. The company distributes to more than 3,000 independent pharmacies, retail drug chains and hospitals, primarily located in the Northeast and Middle Atlantic States. Among products supplied are more than 27,000 individual pharmaceuticals, proprietary medicines, stationery, cosmetics home health care and medical equipment.

The Pharmaceutical Products Distribution Group reported a 15.8% increase in sales between fiscal 1983 and 1984, rising to almost $52 million, of which $2.3 million was attributed to the Toub Distributors acquisition.

The company predicts that sales will continue to rise with the increase of new pharmaceuticals such as antiulcer drugs and beta blockers, and general merchandise like toys and stationery offered through Toub.

While the Healthcare Products Manufacturing Group makes a smaller contribution to overall corporate sales, revenues from this division have been rapidly rising. Between fiscal 1983 and 1984, sales rose by 41.5% to $4.5 million.

This group, which manufactures durable medical equipment under the name of Sci-O-Tech, added several new items during fiscal 1984 and is currently developing a number of others.

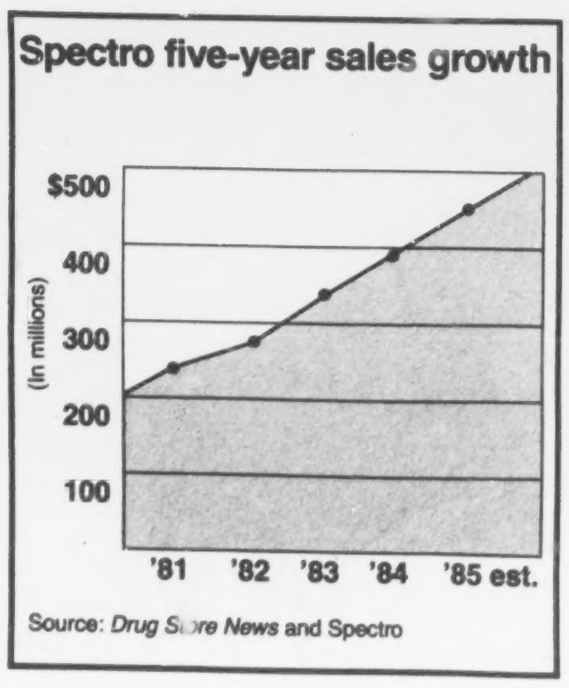
It was also during fiscal 1984, that Spectro saw the solidification of Spectro Medical, an offshoot of the distribution operation that supplies durable medical supplies, exercise equipment and related items to dealers and pharmacists on a same-day basis. Spectro Medical is staffed by professionals who provide training and advice to retailers.

Now, during fiscal 1985, Spectro is involved in the development of a proprietary in-store computer software program for pharmacies, hospitals and durable medical equipment dealers. The company hopes to develop a program to provide a complete inventory and cash control system for pharmacies.

Spectro, itself, is heavily computerized. For example, the majority of the company's customers use Spectro's order-entry system, which is capable of transmitting a 300-item order in seconds. Computers are used in the company's five distribution centers to assemble orders and prepare them for same-day or next-day delivery, while at the same time printing invoices and maintaining perpetual inventories on some 27,000 items.

In the Philadelphia center Spectro uses computerized order-picking machines capable of selecting over 6,000 items an hour.

Computers also allow Spectro to keep track of inventory levels; make use of direct electronic links with suppliers, and provide those suppliers with marketing information about product sales.



PHARMACY

Generics take bigger bite from Rx industry pie

NEW YORK — The sales of generic drugs are surging so strongly that some security analysts are predicting that they will control 30% of the overall prescription market (unit sales) by 1988.

A 30% share of scripts would be double what generics held in 1983 and triple what they did in 1978.

Special report: Generic drugs

Analysts attribute much of the anticipated growth to the generic drug law recently passed by Congress and signed into law by President Reagan.

The new generic drug law grants a number of relatively new drugs extra years of marketing exclusivity. The law's 10-year exclusivity provision applies to any "new" drug which was approved from Jan. 1, 1982 to Sept. 24, 1984, the date the bill became a law. For example, Feldene's patent was slated to expire in 1988, but now the product will enjoy some degree of marketing exclusivity until 1992.

"The generic drug law is the best thing that could happen to the generic drug industry," says Robert Uhl, a research analyst at L. F. Rothschild.

Wall Street analysts are saying that because of the law, the industry can expect to see as many as 125 new generic drugs hit the market in the next two to three years.

Some analysts are estimating that the new generics will generate approximately $1 billion in sales by 1990, making generics a $4 billion industry by the end of this decade.

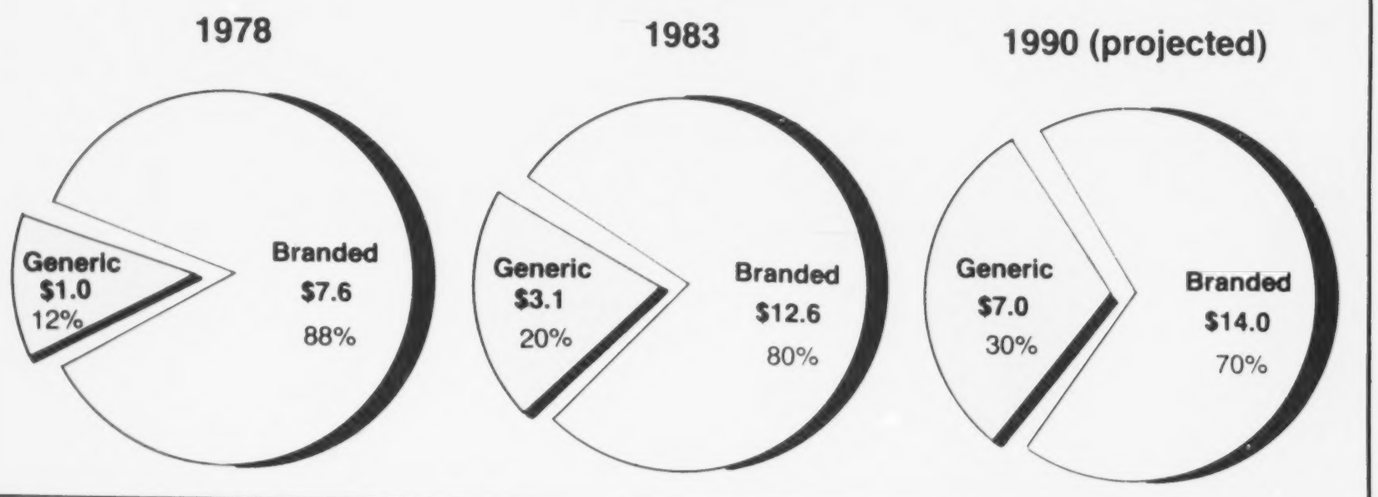
Retailers, too, are positive about the potential for growth, although a few retailers and some wholesalers say that there may be some trade-offs.

Ken Anderson, for instance, vice president and director of Professional Relations at Medicare-Glaser in St. Louis, says the newly passed law will have a staggered impact: it will produce a short-term gain for consumers, followed by some possible long-term trade-offs.

Continued on page 50

Pharmaceutical dollar sales

(in billions)



Source: A. D. Little and Company and industry estimates

THIORIDAZINE HYDROCHLORIDE TABLETS

CONTRAINDICATIONS: In common with other phenothiazines, Thioridazine HCl is contraindicated in severe central nervous system depression or comatose states from any cause. It should also be noted that hypertensive or hypotensive heart disease of extreme degree is a contraindication of phenothiazine administration.

WARNINGS: It has been suggested in regard to phenothiazines in general, that people who have demonstrated a hypersensitivity reaction (e.g., blood dyscrasias, jaundice) to one may be more prone to demonstrate a reaction to others. Attention should be paid to the fact that phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus insecticides. Physicians should carefully consider benefit versus risk when treating less severe disorders.

Reproductive studies in animals and clinical experience to date have failed to show a teratogenic effect with Thioridazine HCl. However, in view of the desirability of keeping the administration of all drugs to a minimum during pregnancy, Thioridazine HCl should be given only when the benefits derived from treatment exceed the possible risks to mother and fetus.

PRECAUTIONS: Leukopenia and/or agranulocytosis and convulsive seizures have been reported but are infrequent. Thioridazine HCl has been shown to be helpful in the treatment of behavioral disorders in epileptic patients, but anticonvulsant medication should also be maintained. Pigmentary retinopathy, which has been observed primarily in patients taking larger than recommended doses, is characterized by diminution of visual acuity, brownish coloring of vision and impairment of night vision; examination of the fundus discloses deposits of pigment. The possibility of this complication may be reduced by remaining within the recommended limits of dosage. Where patients are participating in activities requiring complete mental alertness (e.g., driving) it is advisable to administer the phenothiazines cautiously and to increase the dosage gradually. Female patients appear to have a greater tendency to orthostatic hypotension than male patients. The administration of epinephrine should be avoided in the treatment of drug-induced hypotension in view of the fact that phenothiazines may induce a reversed epinephrine effect on occasion. Should a vasoconstrictor be required, the most suitable are norepinephrine and phenylephrine.

Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

It is recommended that a daily dose in excess of 300 mg. be reserved for use only in severe neuropsychiatric conditions.

ADVERSE REACTIONS: In the recommended dosage ranges with Thioridazine HCl most side effects are mild and transient.

Central Nervous System: Drowsiness may be encountered on occasion, especially where large doses are given early in treatment. Generally, this effect tends to subside with continued therapy or a reduction in dosage. Pseudoparkinsonism and other extrapyramidal symptoms may occur but are infrequent. Nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness and headache have been reported but are extremely rare.

Autonomic Nervous System: Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness and pallor have been seen.

Endocrine System: Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation and peripheral edema have been described.

Skin: Dermatitis and skin eruptions of the urticarial type have been observed infrequently. Photosensitivity is extremely rare.

Cardiovascular System: ECG changes have been reported (see Phenothiazine Derivatives: Cardiovascular Effects).

Other: Rare cases described as parotid swelling have been reported following administration of Thioridazine HCl.

PHENOTHIAZINE DERIVATIVES: *It should be noted that efficacy, indications and untoward effects have varied with the different phenothiazines. It has been reported that old age lowers the tolerance for phenothiazines. The most common neurological side effects in these patients are parkinsonism and akathisia. There appears to be an increased risk of agranulocytosis and leukopenia in the geriatric population. The physician should be aware that the following have occurred with one or more phenothiazines and should be considered whenever one of these drugs is used:*

Autonomic Reactions: Miosis, obstipation, anorexia, paralytic ileus.

Cutaneous Reactions: Erythema, exfoliative dermatitis, contact dermatitis.

Blood Dyscrasias: Agranulocytosis, leukopenia, eosinophilia, thrombocytopenia, anemia, aplastic anemia, pancytopenia.

Allergic Reactions: Fever, laryngeal edema, angioneurotic edema, asthma.

Hepatotoxicity: Jaundice, biliary stasis.

Cardiovascular Effects: Changes in the terminal portion of the electrocardiogram, including prolongation of the Q-T interval, lowering and inversion of the T-wave and appearance of a wave tentatively identified as a bifid T or a U wave have been observed in some patients receiving the phenothiazine tranquilizers, including Thioridazine HCl. To date, these appear to be due to altered repolarization and not related to myocardial damage. They appear to be reversible. While there is no evidence at present that these changes are in any way precursors of any significant disturbance of cardiac rhythm, it should be noted that several sudden and unexpected deaths apparently due to cardiac arrest have occurred in patients previously showing characteristic electrocardiographic changes while taking the drug. The use of periodic electrocardiograms has been proposed but would appear to be of questionable value as a predictive device. Hypotension, rarely resulting in cardiac arrest.

Extrapyramidal Symptoms: Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonus, oculogyric crises, tremor, muscular rigidity, akinesia.

Persistent Tardive Dyskinesia: As with all antipsychotic agents, tardive dyskinesia may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. This risk seems to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities.

There is no known effective treatment for tardive dyskinesia; anti-parkinsonism agents usually do not alleviate the symptoms of this syndrome. It is suggested that all anti-psychotic agents be discontinued if these symptoms appear.

Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, the syndrome may be masked. It has been reported that fine vermicular movements of the tongue may be an early sign of the syndrome and if the medication is stopped at that time, the syndrome may not develop.

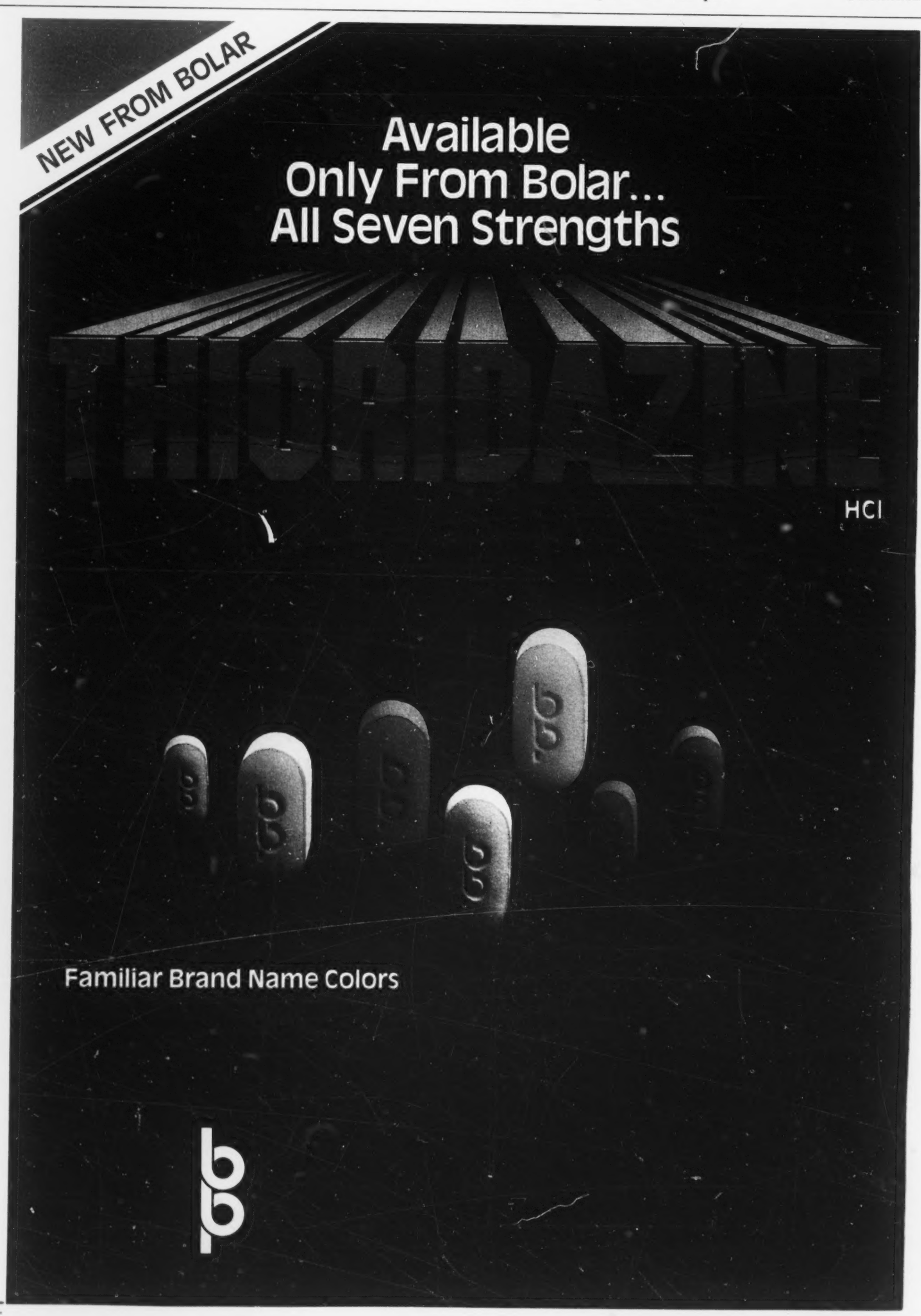
Endocrine Disturbances: Menstrual irregularities, altered libido, gynecomastia, lactation, weight gain, edema. False positive pregnancy tests have been reported.

Urinary Disturbances: Retention, incontinence.

Other: Hyperpyrexia. Behavioral effects suggestive of a paradoxical reaction have been reported. These include excitement, bizarre dreams, aggravation of psychoses and toxic confusional states. More recently, a peculiar skin-eye syndrome has been recognized as a side effect following long-term treatment with phenothiazines. This reaction is marked by progressive pigmentation of areas of the skin or conjunctiva and/or accompanied by discoloration of the exposed sclera and cornea. Opacities of the anterior lens and cornea described as irregular or stellate in shape have also been reported. Systemic lupus erythematosus-like syndrome.

DOSAGE: Dosage must be individualized according to the degree of mental and emotional disturbance. In all cases, the smallest effective dosage should be determined for each patient.

Bolar Pharmaceutical Co., Inc.
Copiague, New York 11726



BEST COPY AVAILABLE

PHARMACY

Dramatic sales growth seen for generic-drug industry

Continued from page 49

"Short term, consumers will receive some real cost savings because additional product availability will force more price competition. In this scenario the law will be a real boom to consumers," he said.

Special report: Generic drugs

But because new products emerging from the research and development pipeline will have an extra five years of patent life, Anderson reasons that consumers will have to wait those additional five years before they can enjoy the price benefits of a generic substitute.

Al Mebane, executive director of the North Carolina Pharmaceutical Association, says that the future reported savings of generics may not be as great as most consumers expect.

"Savings that trace to generic drugs will be balanced against the longer patent life given the innovator of a new drug," he said, "thereby preventing consumers from gaining fast access to generic copies."

But Mebane also acknowledges that the new patented drugs may also carry some residual benefits to consumers in the form of lower introductory prices. This could happen, he reasons, because innovators will have a longer time span in which to recoup developmental costs and enjoy a profit.

Medicare-Glaser's Ken Anderson also sees another advantage to the generic/patent extension bill. He believes the bill will cause manufacturers to work even more closely with retailers, thus creating a "real opportunity to serve the patients and to serve them well."

In the immediate aftermath of the bill becoming law, some sources think the initial savings to consumers will be considerable. William Haddad, president of the Generic Pharmaceutical Association, estimates that prices of major drugs facing competition for the first time will probably be "cut in half immediately, while prices might decrease an additional 20% to 25% as three or four generics hit the market."

Haddad points out that when Librium came off patent, prices dropped from $15 for a bottle of 100 capsules to $1.

Even without the bill, the sales of generics have been steadily increasing. Ottis Calloway, pharmaceutical buyer for Durr-Fillauer Medical, a wholesaler based in Montgomery, Ala., says the firm's generic business has doubled within the past year.

Ken Baily, merchandise manager at Key Wholesaler based in Pittsburgh, says hospitals as well as retailers today are buying many more generic products.

Patent expirations in 1984

Brand name	Manufacturer	Generic name
Ativan	American Home Products	*loraxepam*
Dalmane	Roche	*fluazepam HCl*
Depakene	Abbott	*valproic acid*
Dymelor	Lilly	*acetohexamide*
Inderal	American Home Products	*propranolol HCl*
Navane	Pfizer	*thiothixene*
Restoril	Sandoz	*temazepam*
Serax	American Home Products	*oxazepam*
Diabenese	Pfizer	*chlorpropamide*
Bactrim	Roche	*trimethoprim*
Tinactin	Schering-Plough	*tolnaftate*

Source: U.S. Patent Office

Patent expirations in 1985

Brand name	Manufacturer	Generic name
Aldomet	MSD	*methyldopa*
Desyrel	Mead Johnson	*trazodone HCl*
Motrin	Upjohn	*ibuprofen*
Tranxene	Abbott	*potassium clorzaepate*
Triavil	MSD	*amitriptyline/ perphenazine*
Valium	Roche	*diazepam*

Source: U.S. Patent Office

Patent expirations in 1986

Brand name	Manufacturer	Generic name
Flexeril	MSD	*cyclobenzaprine*
Haldol	Johnson & Johnson	*haloperidol*
Sinequan	Pfizer	*doxepin HCl*
Velosef	Squibb	*cephradine*

Source: U.S. Patent Office

Compact Counter Display Pack
(12s) takes only 2½" of shelf space.
HERPECIN-L®
Cold Sore Lip Balm. *"It Works!"*
Write: CAMPBELL LABORATORIES, INC.
P.O. Box 812-A, FDR, NY, NY 10150

NEW FALL DEAL PLENTIFUL PROFITS

GREAT FALL DEAL!

4 Double-strength sizes to fill your holiday basket with cheer!

Free Goods* Allowance	Plus Advertising Allowance†		Plus Merchandising Allowance		PROMOTIONAL SUPPORT
	OPTION A	OPTION B‡	REDUCED PRICE FEATURE	DISPLAY	
12 oz Liquid 8⅓% Off Invoice	Up to **$1.25** per dozen	**$1.00** per dozen	**$.75** per dozen reduced price feature	**$.75** per dozen floor or end cap display	• Direct to consumer national T.V. promotion . . . 1,250 GRPs June to December 85% Reach 1.2 Billion impressions
5 oz Liquid 8⅓% Off Invoice	Up to **$.75** per dozen	**$.50** per dozen	**$.50** per dozen reduced price feature	**$.50** per dozen floor or end cap display	• Year-round physician detailing and sampling
60s Tablets 8⅓% Off Invoice	Up to **$1.25** per dozen	**$1.00** per dozen	**$.75** per dozen reduced price feature	**$.75** per dozen floor or end cap display	• Major medical and trade journal advertising support
24s Tablets 8⅓% Off Invoice	Up to **$.75** per dozen	**$.50** per dozen	**$.50** per dozen reduced price feature	**$.50** per dozen off-shelf display	

Also Available — Up to **2%** billback allowance for four-color roto advertising or coupon program.
Unlimited purchases allowed for claiming billback allowances.
Retail buy-in period: November 12 through December 21, 1984.
Advertising performance period: November 12, 1984 through February 22, 1985.
Claim deadline: 45 days following appearance of ad.
Contact your Stuart Representative for complete details.

*Through participating wholesaler.
†All ads should feature both liquid and tablet
‡Provided advertising coverage is in at least 75% of the applicant's trading a

© 1984 ICI Americas Inc.

PHARMACY

Pennsylvania warns Rxers on PACE discounts

HARRISBURG, Pa. — The Pennsylvania Department of Aging (DOA) is cracking down on pharmacists who try to build traffic by offering senior citizens discounts, coupons or rebates on copays for prescription products that are already heavily subsidized by the state's new Pharmaceutical Contract to the Elderly (PACE) program.

Fearful that further discounting by retail pharmacists may result in either abuse or overuse of prescription products by the elderly—as well as drive up program costs and possibly the copay—the DOA is threatening to audit and possibly suspend from the PACE program pharmacists who discount the $4 copay to PACE members.

"The offering of discounts, coupons or gifts by pharmacies to entice PACE customers to shop in their stores is strictly prohibited by the PACE agreement," said Carmen A. DiCello, executive director of the Pennsylvania Pharmaceutical Association.

Currently, PACE customers are required to pay a $4 copay for each prescription purchased and it is mandatory for the pharmacist to collect it. DiCello is concerned that any discounts offered to offset the copay would lead to abuse and overutilization of the program.

"If the copay were discounted by the participating pharmacy, I fear many PACE customers would refill prescriptions even if they weren't needed," explains DiCello. "That would drive the cost of the program up and would probably lead to a higher copay."

DiCello says that the PACE program, initiated in July, has been well received by consumer and pharmacist alike. He says it took months of negotiations before PPA and its members were satisfied with the program.

"We've only had reports of about 12 or 13 pharmacies that have offered discounts on the copay," says DiCello. "The DOA and the PPA are not going to let a few rotten apples spoil the program's effectiveness." The DOA hopes early intervention will discourage other pharmacists from violating the program's regulations.

Funds for PACE are provided from the state's lottery. The original proposal was to allot $100 million in lottery funds for three years to support the program. After three years, the costs must be reviewed. The $100 million represents approximately half of the lottery's income.

Even though the program is less than six months old, PACE has become a football in a political playing field.

The program, as it stands today, includes all persons 65 years or older who are making a single income of $9,000 or less or a couple bringing in $12,000 or less. Eligible seniors are signing up for the program at a rate of 7,000-8,000 a month. Thus far, 300,000 persons have signed up for PACE but it is estimated by state officials that there are approximately 700,000 seniors eligible for the program.

But according to DiCello, that number is expected to skyrocket next year when the income limitation is increased to $12,000 for a single person and $15,000 for a couple.

While the announcement of the raise in income limitations came this year, Secretary of Aging, Gorham L. Black Jr. said that applications based on the new ceilings will not be accepted until after Jan. 1, 1985, and will not go into effect until April 1, 1985.

DiCello feels that the raise in the income ceilings will put a strain on the state's budget. He estimates that the additional recipients will cost the state another $120 million dollars and would bring the total eligible seniors to over two million.

Despite the forecast of doom by DiCello the feedback from participating pharmacists has been excellent.

"They think it is a pretty decent program," said DiCello. Some of the items the PPA fought for were: a maximum of 21 days waiting period for payment of claims. After the 21 days, pharmacists are paid with all interest. Also, claims are based on the average wholesale price with no maximum allowable cost clause, as in some other states' regulations. All claims are based on normal product size used for a particular drug.

DiCello is delighted with the outcome of the program because it demonstrated the association's strong political position.

"We went in and fought for our pharmacist," said DiCello. "We're all happy with the compromises that were made."

The current dispensing fee paid to pharmacists in addition to the average wholesale price of the prescription is $2.50, but according to DiCello, a fee of $3 is promised by January.

Correction

In *Drug Store News'* special report on pharmacy computers and POS systems that appeared in the Sept. 17 issue, ComCoTec was misspelled in the "Guide to Hardware Suppliers" and inadvertently left out of the "Guide to Software Versatility."

ComCoTec, headquartered in Westmont, Ill., offers a complete pharmacy software package that runs on Digital Equipment Corp. (DEC) hardware. Included in the basic entry-level price of $19,500 is a hardware/software package that will provide the user with the following functions: label/receipt, patient profile, drug interactions, including drug-to-allergy and drug-to-illness, third-party processing, accounts receivable, perpetual inventory and DEA reports.

The following software enhancements are available at an extra cost: nursing home forms, $1,500; payroll, $1,000; price updates, $30/mo.; durable medical equipment, $1,500; general ledger, $1,500, and accounts payable, $1,500. The total maintenance charge on the software is $50/mo. and includes any enhancements to the system that may be added in the future.

ComCoTec calls its pharmacy computer system RxExpress and it features communication by modem as well as multitasking capabilities.

The RxExpress system will also interface with DTS and Sweda cash registers, making it a complete POS interactive system.

The company plans to offer, in the very near future, an automatic-ordering feature through its POS function.

For more information, write to *ComCoTec Inc., 825 N. Cass Ave., Westmont, Ill. 60559.*

If You Can't Detect 8 Ways To Make This Drug Store More Profitable... Call Us!

Clue #5 Curious customer, but even more curious floor plan.
Clue #3 Did the manager maximize his Rx profits?
Clue #6 The druggist didn't do it, but better third party claims processing might have.
Clue #8 Is there a computer solution in the house?
Clue #7 This clue is old...at least two weeks old.
Clue #4 Who should be putting products on the pegs?
Clue #2 Is the evidence properly merchandised and labeled?
Clue #1 The stock clerk is innocent, but look at the order he's working with.

Answers to Clues:
#1 Economost* – the comprehensive electronic inventory management system, providing easy put-away
#2 Econoplan* – to make sure your shelves promote maximum sales
#3 Econoprice* – for a complete prescription pricing program
#4 COSMcK* – a full service merchandising system
#5 Pharmacy Design – to make sure your stores layout sells products
#6 Econoclaim* – to speed third-party claims processing
#7 OTC Price Update – to keep prices current
#8 Pharmaserve* – for complete computer business solutions

*Registered trademarks of McKesson Drug Company

This small puzzle for drug store professionals is presented by McKesson Drug, providers of state-of-the-art services to the drug store industry. To learn more about any of our scientifically designed services contact your McKesson representative today.

You'll find that making your drug store more profitable... isn't really a big mystery after all.

Another Value-Added™ service from McKesson

McKesson
McKesson Drug Company

© 1984 McKesson Drug Company

PHARMACY

Chains staking claim in home-health market

The list of independent and chain retailers investing in home health care continues to expand dramatically.

To date, at least 18 major chains accounting for approximately 26% of the nation's top 50 chains have begun to chip away at the $3 billion home health care market.

Those include Hook Drug, the nation's 17th largest drug chain, which has 14 freestanding home health care stores; Harco Drug, the 47-unit Northport, Ala.-based chain with nine freestanding stores, and Peoples Drug Stores, the nation's 11th-highest-volume drug chain, which has three freestanding locations.

Other chains with freestanding home health care stores include: Medicare-Glaser, one store; Genovese, one store; Walgreens, three stores; Thrift, one store, and Big B, two.

In addition to those chains with freestanding units, some have in-store departments devoted to home health care—including Revco and Kinney Drug.

Predicasts, a Cleveland-based business information and market research firm, forecasts that the home health care market will reach $5.2 billion in sales by 1988 and top $10 billion by 1995.

Projected growth of the over 65 market

	Population (millions)	65 and over population	% of population 65 & older	Home health expenditures per capita (over 65)
1983	233.9	27.4	11.7	$230
1988	246.0	30.7	12.5	398
1995	260.5	34.0	13.1	731

Source: Predicasts Inc., Cleveland, Ohio

Because of the expected growth, many chains view the home health care business as a means of capturing some of the business they are losing when customers shop for "out-front" merchandise in supermarkets and discount stores.

"I think there is a real opportunity for the chains to make some money in home health care," said Russell Paylor, director of pharmaceutical and home health care products for Peoples Drug. "But we are also aware that it costs more to operate a home health care store."

Most chains are accustomed to operating a payroll between 5% to 10%. But Paylor says Peoples, in its home health care stores, is looking at a payroll that can run as high as 25%-30%.

"This is a service-oriented business," said Paylor. "Somebody has to be on the road all the time to detail the health professionals. That all costs money."

Because opening inventories of a home health care center can run as high as $400,000, many chains are reluctant to open a freestanding unit without first

Continued on page 60

Leading drug chains operating home health care centers

Chain	Headquarters	No. of centers
Hook Drugs Inc.	**Indianapolis**	**14**
Harco Drug Inc.	**Northport, Ala.**	**8**
Begley Drug Co.	**Richmond, Ky.**	**5**
Peoples Drug Stores	**Alexandria, Va.**	**3**
The Walgreen Co.	**Deerfield, Ill.**	**3**
Jack Eckerd Corp.	**Largo, Fla.**	**3**
Big B Inc.	**Birmingham, Ala.**	**2**
Medicare-Glaser	**St. Louis, Mo.**	**1**
Genovese Drug Stores	**Melville, N.Y.**	**1**
Thrift Drug Co.	**Pittsburgh, Pa.**	**1**
Happy Harry's	**Newark, Del.**	**1**
SupeRx Drugs	**Cincinnati**	**1**
Tiffany Davis	**Eugene, Ore.**	**1**

Source: *Drug Store News* survey

BEST COPY AVAILABLE

BRIEF SUMMARIES

DIPYRIDAMOLE TABLETS

INDICATIONS: Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indication as follows: Possibly effective for long term therapy of chronic angina pectoris. Prolonged therapy may reduce the frequency or eliminate anginal episodes, improve exercise tolerance, and reduce nitroglycerin requirements. The drug is not intended to abort the acute anginal attack. Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS: No specific contraindications are known. **PRECAUTIONS**: Since excessive doses can produce peripheral vasodilation, the drug should be used cautiously in patients with hypotension. **ADVERSE REACTIONS**: Adverse reactions are minimal and transient to recommended dosages. Instances of headache, dizziness, nausea, flushing, weakness or syncope, mild gastrointestinal distress and skin rash have been noted during therapy. Rare cases of what appeared to be an aggravation of angina pectoris have been reported, usually at the initiation of therapy. On those uncommon occasions when adverse reactions have been persistent or intolerable to the patient, withdrawal of the medication has been followed promptly by cessation of the undesirable symptoms.

FUROSEMIDE TABLETS

WARNING: Furosemide is a potent diuretic which, if given in excessive amounts, can lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose and dose schedule have to be adjusted to the individual patient's needs. (See under "DOSAGE AND ADMINISTRATION.")

INDICATIONS: Edema—Furosemide is indicated for the treatment of edema associated with congestive heart failure, cirrhosis of the liver, and renal disease, including the nephrotic syndrome. Furosemide is particularly useful when an agent with greater diuretic potential than that of those commonly employed is desired. Furosemide is indicated as adjunctive therapy in acute pulmonary edema. Hypertension—Furosemide may be used for the treatment of hypertension alone or in combination with other antihypertensive agents. Hypertensive patients who cannot be adequately controlled with thiazides will probably also not be adequately controlled with furosemide alone. **CONTRAINDICATIONS**: Furosemide is contraindicated in anuria. It is contraindicated in patients with a history of hypersensitivity to this compound. **WARNINGS**: Excessive diuresis may result in dehydration and reduction in blood volume with circulatory collapse and with the possibility of vascular thrombosis and embolism, particularly in elderly patients. Excessive loss of potassium in patients receiving digitalis glycosides may precipitate digitalis toxicity. Care should also be exercised in patients receiving potassium-depleting steroids. Frequent serum electrolyte, CO_2, and BUN determinations should be performed during the first few months of therapy and periodically thereafter, and abnormalities corrected or the drug temporarily withdrawn. In patients with hepatic cirrhosis and ascites, initiation of therapy with furosemide is best carried out in the hospital. In hepatic coma and in states of electrolyte depletion, therapy should not be instituted until the basic condition is improved. Sudden alterations of fluid and electrolyte balance in patients with cirrhosis may precipitate hepatic coma; therefore, strict observation is necessary during the period of diuresis. Supplemental potassium chloride and, if required, an aldosterone antagonist are helpful in preventing hypokalemia and metabolic alkalosis. If increasing azotemia and oliguria occur during treatment of severe progressive renal disease, the drug should be discontinued. As with many other drugs, patients should be observed regularly for the possible occurrence of blood dyscrasias, liver damage, or other idiosyncratic reactions. Patients with known sulfonamide sensitivity may show allergic reactions to furosemide. Furosemide may add to or potentiate the therapeutic effect of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs. The possibility exists of exacerbation or activation of systemic lupus erythematosus. Furosemide appears in breast milk. If use of the drug is deemed essential, the patient should stop nursing. **PRECAUTIONS**: As with any effective diuretic, electrolyte depletion may occur during therapy with furosemide, especially in patients receiving higher doses and a restricted salt intake. Periodic determination of serum electrolytes to detect possible imbalance should be performed at appropriate intervals. All patients receiving furosemide therapy should be observed for signs of fluid or electrolyte imbalance; namely hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medications such as digitalis may also influence serum electrolytes. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, arrhythmia, and gastrointestinal disturbances such as nausea and vomiting. Hypokalemia may develop with furosemide as with any other potent diuretic, especially with brisk diuresis, when cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity. Asymptomatic hyperuricemia can occur and gout may rarely be precipitated. Periodic checks on urine and blood glucose should be made in diabetics and even those suspected of latent diabetes when receiving furosemide. Increases in blood glucose and alterations in glucose tolerance tests with abnormalities of the fasting and 2-hour postprandial sugar have been observed and rare cases of precipitation of diabetes mellitus have been reported. Furosemide may lower serum calcium levels and rare cases of tetany have been reported. Accordingly, periodic serum calcium levels should be obtained. Reversible elevations of BUN may be seen. These have been observed in association with dehydration, which should be avoided, particularly in patients with renal insufficiency. Patients receiving high doses of salicylates, as in rheumatic disease, in conjunction with furosemide may experience salicylate toxicity at lower doses because of competitive renal excretory sites. Furosemide has a tendency to antagonize the skeletal muscle relaxing effect of tubocurarine and may potentiate the action of succinylcholine. Lithium generally should not be given with diuretics because they reduce its renal clearance and add a high risk of lithium toxicity. It has been reported in the literature that diuretics such as furosemide may enhance the nephrotoxicity of cephaloridine. Therefore, furosemide and cephaloridine should not be administered simultaneously. Furosemide may decrease arterial responsiveness to norepinephrine. This diminution is not sufficient to preclude effectiveness of the pressor agent for therapeutic use. It has been reported in the literature that coadministration of indomethacin may reduce the natriuretic and antihypertensive effects of furosemide in some patients. This effect has been attributed to inhibition of prostaglandin synthesis by indomethacin. Indomethacin may also affect plasma renin levels and aldosterone excretion; this should be borne in mind when a renin profile is evaluated in hypertensive patients. Patients receiving both indomethacin and furosemide should is achieved. **Pregnancy**: Pregnancy Category C. Furosemide has been shown to cause unexplained maternal deaths and abortions in rabbits at 2, 4 and 8 times the human dose. There are no adequate and well-controlled studies in pregnant women. Furosemide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. The effects of furosemide on embryonic and fetal development and on pregnant dams were studied in mice, rats and rabbits. Furosemide caused unexplained maternal deaths and abortions in the rabbit when 50 mg/kg (4 times the maximal recommended human dose of 600 mg/day) was administered between days 12 and 17 of gestation. In a previous study the lowest dose of only 25 mg/kg (2 times the maximal recommended human dose of 600 mg/day) caused maternal deaths and abortions. In a third study, none of the pregnant rabbits survived a dose of 100 mg/kg. Data from the above studies indicate fetal lethality that can precede materanl deaths. The results of the mouse study and one of the three rabbit studies also showed an increased incidence of hydronephrosis (distention of the renal pelvis and, in some cases, of the ureters) in fetuses derived from treated dams as compared to the incidence in fetuses from the control group.

ADVERSE REACTIONS

Gastrointestinal System Reactions

1. anorexia, 2. oral and gastric irritation, 3. nausea, 4. vomiting, 5. cramping, 6. diarrhea, 7. constipation, 8. jaundice (intrahepatic cholestatic jaundice), 9. pancreatitis.

Central Nervous System Reactions

1. dizziness, 2. vertigo, 3. paresthesias, 4. headache, 5. xanthopsia, 6. blurred vision, 7. tinnitus and hearing loss.

Hematologic Reactions

1. anemia, 2. leukopenia, 3. agranulocytosis (rare), 4. thrombocytopenia, 5. aplastic anemia (rare).

Dermatologic—Hypersensitivity Reactions

1. purpura, 2. photosensitivity, 3. rash, 4. urticaria, 5. necrotizing angiitis (vasculitis, cutaneous vasculitis), 6. exfoliative dermatitis, 7. erythema multiforme, 8. pruritus.

Cardiovascular Reaction

Orthostatic hypotension may occur and be aggravated by alcohol, barbiturates, or narcotics.

Other

1. hyperglycemia, 2. glycosuria, 3. hyperuricemia, 4. muscle spasm, 5. weakness, 6. restlessness, 7. urinary bladder spasm, 8. thrombophlebitis.

Whenever adverse reactions are moderate or severe, furosemide dosage should be reduced or therapy withdrawn.

METRONIDAZOLE

WARNING

Metronidazole has been shown to be carcinogenic in mice and rats. (See WARNINGS.) Unnecessary use of this drug should be avoided. Its use should be reserved for the conditions described in the **INDICATIONS** section below.

INDICATIONS AND USAGE: **Symptomatic Trichomoniasis** Metronidazole is indicated for the treatment of symptomatic trichomoniasis in females and males when the presence of trichomonad has been confirmed by appropriate laboratory procedures (wet smears and/or cultures). **Asymptomatic Trichomoniasis**: Metronidazole is indicated in the treatment of asymptomatic females when the organism is associated with endocervicitis, cervicitis, or cervical erosion. Since there is evidence that presence of the trichomonad can interfere with accurate assessment of abnormal cytological smears, additional smears should be performed after eradication of the parasite. **Treatment of Asymptomatic Consorts**: **T. vaginalis** infection is a venereal disease. Therefore, asymptomatic sexual partners of treated patients should be treated simultaneously if the organism has been found to be present in order to prevent reinfection of the partner. The decision as to whether to treat an asymptomatic male partner with a negative culture or one in whom no culture has been attempted is an individual one. In making this decision, it should be noted that there is evidence that there can be considerable difficulty in isolating the organism from the asymptomatic male carrier; negative smears and cultures cannot be relied upon in this regard. In any event, the consort should be treated with Metronidazole in cases of reinfection. **Amebiasis**: Metronidazole is indicated in the treatment of acute intestinal amebiasis (amebic dysentery) and amebic liver abscess. In amebic liver abscess, Metronidazole therapy does not obviate the need for aspiration or drainage of pus. **Anaerobic Bacterial Infections**: Treatment with Metronidazole is indicated in serious anaerobic infections caused by susceptible anaerobic bacteria. Metronidazole is rapid in its bactericidal action against susceptible anaerobes, is broad in spectrum against common anaerobic bacteria and shows penetration into closed-space infections and essentially all body tissues, fluids and cavities. (3, 11) Metronidazole therapy should be performed in conjunction with appropriate surgical procedures or concomitant treatment of predisposing conditions which favor anaerobiasis. (5, 6, 10) Anaerobic infections are most often polymicrobic, with combinations of aerobic, facultative, and anaerobic species (10). Antibiotics appropriate for the treatment of the anaerobic or facultative species isolated should be used in conjunction with Metronidazole therapy. The table below lists anaerobic infections clinically proven to respond to Metronidazole therapy. 4, 9, 12, 13, 14) INTRA-ABDOMINAL INFECTIONS, including peritonitis, intra-abdominal abscess, and liver abscess, caused by **Bacteroides** species including the ***B. fragilis*** group (***B. fragilis, B. distasonis, B. ovatus, B. thetaiotaomicron, B. vulgatus***); ***Clostridium*** species; ***Eubacterium*** species; ***Peptococcus*** species; and ***Peptostreptococcus*** species. SKIN AND SKIN STRUCTURE INFECTIONS caused by ***Bacteroides*** species including the ***B. fragilis*** group; ***Clostridium*** species; ***Peptococcus*** species; ***Peptostreptococcus*** species; and ***Fusobacterium*** species. GYNECOLOGIC INFECTIONS, including endometritis, endomyometritis, tubo-ovarian abscess, and post-surgical vaginal cuff infection, caused by ***Bacteroides*** species including the ***B. fragilis*** group; ***Clostridium*** species; ***Peptococcus*** species; and ***Peptostreptococcus*** species. BACTERIAL SEPTICEMIA caused by ***Bacteroides*** species including the ***B. fragilis*** group; and ***Clostridium*** species. BONE AND JOINT INFECTIONS, as adjunctive therapy, caused by ***Bacteroides*** species including the ***B. fragilis*** group. CENTRAL NERVOUS SYSTEM (CNS) INFECTIONS, including meningitis and brain abscess, caused by ***Bacteroides*** species including the ***B. fragilis*** group. LOWER RESPIRATORY TRACT INFECTIONS, including pneumonia, empyema, and lung abscess, caused by ***Bacteroides*** species including the ***B. fragilis*** group. ENDOCARDITIS caused by ***Bacteroides*** species including the ***B. fragilis*** group. **CONTRAINDICATIONS**: Metronidazole is contraindicated during the first trimester of pregnancy. (**SEE WARNINGS.**) Metronidazole is also contraindicated in patients with a prior history of hypersensitivity to Metronidazole. **WARNINGS**: **Convulsive Seizures and Peripheral Neuropathy** Convulsive seizures and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity, have been reported in patients treated with Metronidazole. The appearance of abnormal neurologic signs demands the prompt discontinuation of Metronidazole therapy. Metronidazole should be administered with caution if at all, to patients with central nervous system diseases. This decision should be based on a benefit/risk assessment of the condition to be treated. Metronidazole has shown evidence of carcinogenic activity in a number of studies involving chronic, oral administration in mice and rats. Prominent among the effects in the mouse was the promotion of pulmonary tumorigenesis. This has been observed in all six reported studies in the species, including one study in which the animals were dosed on an intermittent schedule (administration during every fourth week only). At very high dose levels (approx. 500 mg/kg/day) there was a statistically significant increase in the incidence of malignant liver tumors in males. Also, the published results of one of the mouse studies indicate an increase in the incidence of malignant lymphomas as well as pulmonary neoplasms associated with lifetime feeding of the drug. All these effects are statistically significant. Several long-term oral-dosing studies in the rats have been completed. There was a statistically significant increase in the incidence of various neoplasms, particularly in mammary and hepatic tumors, among female rats administered Metronidazole over those noted in the concurrent female control groups. Two lifetime tumorigenicity studies in hamsters have been performed and reported to be negative. **Mutagenicity Studies**: Although Metronidazole has shown mutagenic activity in a number of **in vitro** assay systems, studies in mammals (**in vivo**) have failed to demonstrate a potential for genetic damage. **PRECAUTIONS**: General: Patients with severe hepatic disease metabolize Metronidazole slowly, with resultant accumulation of Metronidazole and its metabolites in the plasma. Accordingly, for such patients, doses below those usually recommended should be administered cautiously. Known or previously unrecognized candidiasis may present more prominent symtoms during therapy with Metronidazole and requires treatment with a candicidal agent. **Laboratory Tests**: Metronidazole is a nitroimidazole and should be used with care in patients with evidence of, or history of blood dycrasia. A mild leukopenia has been observed during its administration; however, no persistent hematologic abnormalities attributable to Metronidazole have been observed in clinical studies. Total and differential leukocyte counts are recommended before and after therapy for trichomoniasis and amebiasis, especially if a second course of therapy is necessary. **Drug Interactions**: Metronidazole has been reported to potentiate the anticoagulant effect of coumadin and warfarin resulting in a prolongation of prothrombin time. This possible drug interaction should be considered when Metronidazole is prescribed for patients on this type of anticoagulant therapy. Alcohol beverages should not be consumed during Metronidazole therapy because abdominal cramps, nausea, vomiting, headache, and flushing may occur. **Drug Laboratory Test Interactions**: Metronidazole may interfere with certain chemical analyses for serum glutamic oxalacetic transaminase, resulting in decreased values. Values of zero may be observed. **Carcinogenesis**: (**SEE WARNINGS.**) **Pregnancy**: **Teratogenic Effects—Pregnancy Category B**: Metronidazole crosses the placental barrier and enters the fetal circulation rapidly. Reproduction studies have been performed in rabbits and rats at doses up to five times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Metronidazole. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, and because Metronidazole is a carcinogen in rodents, this drug should be used during pregnancy only if clearly needed (SEE CONTRAINDICATIONS). Use of Metronidazole for trichomoniasis in the second and third trimesters should be restricted to those in whom local palliative treatment has been inadequate to control symptoms. **Nursing Mothers**: Because of the potential for tumorigenicity shown for Metronidazole in mouse and rat studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Metronidazole is secreted in breast milk in concentrations similar to those found in plasma. **Pediatric use**: Safety and effectiveness in children have not been established, except for the treatment of amebiasis. **ADVERSE REACTIONS**: The two most serious adverse reactions reported in patients treated with metronidazole have been convulsive seizures and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity. Since persistent peripheral neuropathy has been reported in some patients receiving prolonged administration of metronidazole, patients should be specifically warned about these reactions and should be told to stop the drug and report immediately to their physicians if any neurologic symptoms occur. The most common advese reactions reported have been referable to the gastrointestinal tract, particularly nausea, sometimes accompanied by headache, anorexia, and occasionally vomiting, diarrhea, epigastric distress, and abdominal cramping. Constipation has also been reported. The following reactions have also been reported during treatment with metronidazole: **Mouth**: A sharp, unpleasant metallic taste is not unusual. Furry tongue, glossitis, and stomatitis have occurred; these may be associated with a sudden overgrowth of ***Candida*** which may occur during effective therapy. **Hematopoietic**: Reversible neutropenia (leukopenia). **Cardiovascular**: Flattening of the T wave may be seen in electrocardiographic tracings. **Central Nervous System**: Convulsive seizures, peripheral neuropathy, dizziness, vertigo, incoordination, ataxia, confusion, irritability, depression, weakness, and insomnia. **Hypersensitivity**: Urticaria, erythematous rash, flushing, nasal congestion, dryness of mouth (or vagina or vulva), and fever. **Renal**: Dysuria, cystitis, polyuria, incontinence, and a sense of pelvic pressure. Instances of darkened urine have been reported, and this manifestation has been the subject of a special investigation. Although the pigment which is probably responsible for this phenomenon has not been positively identified, it is almost certainly a metabolite of metronidazole and seems to have no clinical significance. **Other**: Proliferation of ***Candida*** in the vagina, dyspareunia, decrease of libido, proctitis, and fleeting joint pains sometimes resembling serum sickness. If patients receiving metronidazole drink alcoholic beverages, they may experience abdominal distress, nausea, vomiting, flushing, or headache. A modification of the taste of alcoholic beverages has also been reported.

SPIRONOLACTONE

WARNING: Spironolactone has been shown to be a tumorigen in chronic toxicity studies in rats (see warnings.) Spironolactone should be used only in those conditions described under indications. Unnecessary use of this drug should be avoided.

INDICATIONS: Spironolactone is indicated in the management of: **Primary hyperaldosteronism for** Establishing the diagnosis of primary hyperaldosteronism by therapeutic trial. Short-term preoperative treatment of patients with primary hyperaldosteronism. Long-term maintenance therapy for patients with discrete aldosterone-producing adrenal adenomas who are judged to be poor operative risks, or who decline surgery. Long-term maintenance therapy for patients with bilateral micro- or macro-nodular adrenal hyperplasia (idiopathic hyperaldosteronism). **Edematous conditions for patients with**: Congestive heart failure. For the management of edema and sodium retention when the patient is only partially responsive to, or is intolerant of, other therapeutic measures. Spironolactone is also indicated for patients with congestive heart failure taking digitalis when other therapies are considered inappropriate. **Cirrhosis of the liver accompanied by edema and/or ascites**: Aldosterone levels may be exceptionally high in this condition. Spironolactone is indicated for maintenance therapy together with bed rest and the restriction of fluid and sodium. **The nephrotic syndrome**: For nephrotic patients when treatment of the underlying disease, restriction of fluid and sodium intake, and the use of other diuretics do not provide an adequate response. **Essential Hypertension**: Usually in combination with other drugs. Spironolactone is indicated for patients who cannot be treated adequately with other agents or for whom other agents are considered inappropriate. **Hypokalemia**: For the treatment of patients with hypokalemia when other measures are considered inappropriate or inadequate. Spironolactone is also indicated for the prophylaxis of hypokalemia in patients taking digitalis when other measures are considered inadequate or inappropriate. **Usage in Pregnancy**: The routine use of diuretics in an otherwise healthy woman is inappropriate and exposes mother and fetus to unnecessary hazard. Diuretics do not prevent development of toxemia of pregnancy, and there is no satisfactory evidence that they are useful in the treatment of developing toxemia. Edema during pregnancy may arise from pathologic causes just as it is in the absence of pregnancy (however, see WARNINGS section). Dependent edema in pregnancy, resulting from restriction of venous return by the expanded uterus, is properly treated through elevation of the lower extremities and use of support hose; use of diuretics to lower intravascular volume in this case is unsupported and unnecessary. There is hypervolemia during normal pregnancy which is harmful to neither the fetus nor the mother (in the absence of cardiovascular disease), but which is associated with edema, including generalized edema, in the majority of pregnant women. If this edema produces discomfort, increased recumbency will often provide relief. In rare instances, this edema may cause extreme discomfort which is not relieved by rest. In these cases, a short course of diuretics may provide relief and may be appropriate. **CONTRAINDICATIONS**: Spironolactone is contraindicated for patients with anuria, acute renal insufficiency, significant impairment of renal function, or hyperkalemia. **WARNINGS**: Potassium supplementation, either in the form of medication or as a diet rich in potassium, should not ordinarily be given in association with Spironolactone therapy. Excessive potassium intake may cause hyperkalemia in patients receiving Spironolactone (see Precautions section). Spironolactone should not be administered with other potassium-sparing diuretics. Spironolactone has been shown to be a tumorigen in chronic toxicity studies performed in rats, with its proliferative effects manifested on endocrine organs and the liver. In one study using 25, 75 and 250 times the usual daily human dose (2 mg/kg) there was a statistically significant dose-related increase in benign adenomas of the thyroid and testes. In female rats there was a statistically significant increase in malignant mammary tumors at the mid-dose only. In male rats there was a dose-related increase in proliferative changes in the liver. At the highest dosage level (500 mg/kg) the range of effects included hepatocytomegaly, hyperplastic nodules and hepatocellular carcinoma; the last was not statistically significant at a value of $p = 0.05$. **PRECAUTIONS**: Because of the diuretic action of Spironolactone, patients should be carefully evaluated for possible disturbances of fluid and electrolyte balance. Hyperkalemia may occur in patients with impaired renal function or excessive potassium intake and can cause cardiac irregularities which may be fatal. Consequently, no potassium supplement should ordinarily be given with spironolactone with hydrochlorothiazide. Hyperkalemia can be treated promptly by rapid intravenous administration of glucose (20 to 50 percent) and regular insulin, using 0.25 to 0.5 units of insulin per gram of glucose. This is a temporary measure to be repeated as required. Spironolactone with hydrochlorothiazide should be discontinued and potassium intake (including dietary potassium) restricted. Hypokalemia may develop as a result of profound diuresis, particularly when spironolactone with hydrochlorothiazide is used concomitantly with loop diuretics, glucocorticoids or ACTH. Hypokalemia may exaggerate the effects of digitalis therapy. Potassium depletion may induce signs of digitalis intoxication at previously tolerated dosage levels. Warning signs of possible fluid and electrolyte imbalance include dryness of the mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia and gastrointestinal symptoms. Spironolactone with hydrochlorothiazide therapy may cause a transient elevation of BUN. This appears to represent a concentration phenomenon rather than renal toxicity, since the BUN returns to normal after Spironolactone with hydrochlorothiazide is discontinued. Progressive elevation BUN is suggestive of the presence of pre-existing renal impairment. Dilutional hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, and confirmed by a low serum sodium level, may be induced, especially when spironolactone with hydrochlorothiazide is administered in combination with other diuretics. A true low-salt syndrome may rarely develop with spironolactone with hydrochlorothiazide therapy and may be manifested by increasing mental confusion similar to that observed with hepatic coma. This syndrome is differentiated from dilutional hyponatremia in that it does occur with obvious fluid retention. Its treatment requires that diuretic therapy be discontinued and sodium administered. Gynecomastia may develop in association with the use of spironolactone, and physicians should be alert to its possible onset. The development of gynecomastia appears to be related to both dosage level and duration of therapy and is normally reversible when Spironolactone with hydrochlorothiazide is discontinued. In rare instances some breast enlargement may persist. Thiazides have been demonstrated to alter the metabolism of uric acid and carbohydrates, with possible development of hyperuricemia, gout and decreased glucose tolerance. Thiazides may temporarily exaggerate abnormalities of glucose metabolism in diabetic patients or cause abnormalities to appear in patients with latent diabetes. Both spironolactone and hydrochlorothiazide reduce the vascular responsiveness to norepinephrine. Therefore, caution should be exercised in the management of patients subjected to regional or general anesthesia while they are being treated with spironolactone with hydrochlorothiazide. Thiazides may also increase the responsiveness to tubocurarine. The antihypertensive effects of hydrochlorothiazide may be enhanced in patients who have undergone sympathectomy. Pathologic changes in the parathyroid gland with hypercalcemia and hypophosphatemia have been observed in patients on prolonged thiazide therapy. Thiazides may also decrease serum PBI levels without evidence of alteration of thyroid function. **USAGE IN PREGNANCY**: Spironolactone or its metabolites may, and hydrochlorothiazide does, cross the placental barrier. Therefore, the use of it in pregnant women requires that the anticipated benefit be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possible other adverse reactions which have been reported in the adult. **NURSING MOTHERS**: Canrenone, a metabolite of spironolactone, and hydrochlorothiazide appear in breast milk. If use of these drugs is deemed essential, an alternative method of infant feeding should be instituted. **ADVERSE REACTIONS**: Gynecomastia is observed not infrequently. Other adverse reactions that have been reported in association with the use of spironolactone are: gastrointestinal symptoms including cramping and diarrhea; drowsiness, lethargy, headache; maculopapular or erythematous cutaneous eruptions; urticaria; mental confusion; drug fever; ataxia; inability to achieve or maintain erection; irregular menses or amenorrhea; postmenopausal bleeding; hirsutism and deepening of the voice. Carcinoma of the breast has been reported in patients taking spironolactone, but a cause and effect relationship has not been established. Adverse reactions reported in association with the use of thiazides include: **A. Gastrointestinal System**: 1. Anorexia, 2. gastric irritation, 3. nausea, 4. vomiting, 5. cramping, 6. diarrhea, 7. constipation, 8. jaundice (intrahepatic cholestatic jaundice), 9. pancreatitis, 10. sialadenitis. **B. Central Nervous System**: 1. dizziness, 2. vertigo, 3. paresthesia, 4. headache, 5. xanthopsia. **C. Hematologic**: 1. leukopenia, 2. agranulocytosis, 3. thrombocytopenia, 4. aplastic anemia. **D. Cardiovascular**: 1. orthostatic hypotension (may be aggravated by alcohol, barbiturates, or narcotics). **E. Hypersensitivity**: 1. purpura, 2. photosensitivity, 3. rash, 4. urticaria, 5. necrotizing angiitis (vasculitis) (cutaneous vasculitis), 6. fever, 7. anaphylactic reactions, 8. respiratory distress, including pneumonitis. **F. Other**: 1. hyperglycemia, 2. glycosuria, 3. hyperuricemia, 4. muscle spasm, 5. weakness, 6. restlessness, 7. transient blurred vision. Whenever adverse reactions are moderate or severe, hydrochlorothiazide dosage should be reduced or therapy withdrawn.

SPIRONOLACTONE WITH HYDROCHLOROTHIAZIDE

WARNING

Spironolactone has been shown to be a tumorigen in chronic toxicity studies in rats (see warnings.) Spironolactone should be used only in those conditions under indications. Unnecessary use of this drug should be avoided.

Fixed-dose combination drugs are not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be re-evaluated as conditions in each patient warrant.

INDICATIONS: Spironolactone has been shown to be a tumorigen in chronic toxicity studies in rats (see Warnings section). Spironolactone should be used only in those conditions described below. Unnecessary use of this drug should be avoided. Spironolactone with Hydrochlorothiazide is indicated for: **Edematous conditions for patients with: Congestive heart failure**: For the management of edema and sodium retention when the patient is only partially responsive to, or is intolerant of other therapeutic measures. The treatment of diuretic-induced hypokalemia in patients with congestive heart failure when other measures are considered inappropriate. The treatment of patients with congestive heart failure taking digitalis when other therapies are considered inadequate or inappropriate. **Cirrhosis of the liver accompanied by edema and/or ascites**: Aldosterone levels may be exceptionally high in this condition. Spironolactone with hydrochlorothiazide is indicated for maintenance therapy together with bed rest and the restriction of fluid and sodium. **The nephrotic syndrome**: For nephrotic patients when treatment of the underlying disease, restriction of fluid and sodium intake, and the use of other diuretics do not provide an adequate response. **Essential Hypertension**: For patients with essential hypertension in whom other measures are considered inadequate or inappropriate. In hypertensive patients for the treatment of a diuretic-induced hypokalemia when other measures are considered inappropriate. **USAGE IN PREGNANCY**: The routine use of diuretics in an otherwise healthy woman is inappropriate and exposes mother and fetus to unnecessary hazard. Diuretics do not prevent development of toxemia of pregnancy, and there is no satisfactory evidence that they are useful in the treatment of developing toxemia. Edema during pregnancy may arise from pathologic causes or from the physiologic and mechanical consequences of pregnancy. Spironolactone with hydrochlorothiazide is indicated in pregnancy when edema is due to pathologic causes just as it is in the absence of pregnancy (however, see Warnings section). Dependent edema in pregnancy, resulting from restriction of venous return by the expanded uterus, is properly treated through elevation of the lower extremities and use of support hose; use of diuretics to lower intravascular volume in this case is unsupported and unnecessary. There is hypervolemia during normal pregnancy which is harmful to neither the fetus or the mother (in the absence of cardiovascular disease), but which is associated with edema, including generalized edema in the majority of pregnant women. If this edema produces discomfort, increased recumbency will often provide relief. In rare instances, this edema may cause extreme discomfort which is not relieved by rest. In these cases, a short course of diuretics may provide relief and may be appropriate. **CONTRAINDICATIONS**: Spironolactone with hydrochlorothiazide is contraindicated in patients with anuria, acute renal insufficiency, significant impairment of renal function or hyperkalemia, and in patients who are allergic to thiazide diuretics or to other sulfonamide-derived drugs. Spironolactone with hydrochlorothiazide may also be contraindicated in acute or severe hepatic failure. **WARNINGS**: Potassium supplementation, either in the form of medication or as a diet rich in potassium, should not ordinarily be given in association with spironolactone with hydrochlorothiazide therapy. Excessive potassium intake may cause hyperkalemia in patients receiving spironolactone with hydrochlorothiazide (see Precautions section). Spironolactone with hydrochlorothiazide should not be administered concurrently with other potassium-sparing diuretics. Sulfonamide derivatives, including thiazides, have been reported to exacerbate or activate systemic lupus erythematosus. Spironolactone has been shown to be a tumorigen in chronic toxicity studies performed in rats, with its proliferative effects manifested on endocrine organs and the liver. In one study using 25, 75 and 250 times the usual daily human dose (2 mg/kg) there was a statistically significant dose-related increase in benign adenomas of the thyroid and testes. In female rats there was a statistically significant increase in malignant mammary tumors at the mid-dose only. In male rats there was a dose-related increase in proliferative changes in the liver. At the highest level (500 mg/kg) the range at effects included hepatocytomegaly, hyperplastic nodules and hepatocellular carcinoma; the last was not statistically significant at a value of $p = 0.05$. **PRECAUTIONS**: Patients receiving spironolactone with hydrochlorothiazide therapy should be carefully evaluated for possible disturbances of fluid and electrolyte balance. Hyperkalemia may occur in patients with impaired renal function or excessive potassium intake and can cause cardiac irregularities which may be fatal. Consequently, no potassium supplement should ordinarily be given with spironolactone with hydrochlorothiazide. Hyperkalemia can be treated promptly by rapid intravenous administration of glucose (20 to 50 percent) and regular insulin, using 0.25 to 0.5 units of insulin per gram of glucose. This is a temporary measure to be repeated as required. Spironolactone with hydrochlorothiazide should be discontinued and potassium intake (including dietary potassium) restricted. Hypokalemia may develop as a result of profound diuresis, particularly when spironolactone with hydrochlorothiazide is used concomitantly with loop diuretics, glucocorticoids or ACTH. Hypokalemia may exaggerate the effects of digitalis therapy. Potassium depletion may induce signs of digitalis intoxication at previously tolerated dosage levels. Warning signs of possible fluid and electrolyte imbalance include dryness of the mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia and gastrointestinal symptoms. Spironolactone with hydrochlorothiazide therapy may cause a transient elevation of BUN. This appears to represent a concentration phenomenon rather than renal toxicity, since the BUN returns to normal after Spironolactone with hydrochlorothiazide is discontinued. Progressive elevation BUN is suggestive of the presence of pre-existing renal impairment. Dilutional hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, and confirmed by a low serum sodium level, may be induced, especially when spironolactone with hydrochlorothiazide is administered in combination with other diuretics. A true low-salt syndrome may rarely develop with spironolactone with hydrochlorothiazide therapy and may be manifested by increasing mental confusion similar to that observed with hepatic coma. This syndrome is differentiated from dilutional hyponatremia in that it does occur with obvious fluid retention. Its treatment requires that diuretic therapy be discontinued and sodium administered. Gynecomastia may develop in association with the use of spironolactone, and physicians should be alert to its possible onset. The development of gynecomastia appears to be related to both dosage level and duration of therapy and is normally reversible when Spironolactone with hydrochlorothiazide is discontinued. In rare instances some breast enlargement may persist. Thiazides have been demonstrated to alter the metabolism of uric acid and carbohydrates, with possible development of hyperuricemia, gout and decreased glucose tolerence. Thiazides may temporarily exaggerate abnormalities of glucose metabolism in diabetic patients or cause abnormalities to appear in patients with latent diabetes. Both spironolactone and hydrochlorothiazide reduce the vascular responsiveness to norepinephrine. Therefore, caution should be exercised in the management of patients subjected to regional or general anesthesia while they are being treated with spironolactone with hydrochlorothiazide. Thiazides may also increase the responsiveness to tubocurarine. The antihypertensive effects of hydrochlorothiazide may be enhanced in patients who have undergone sympathectomy. Pathologic changes in the parathyroid gland with hypercalcemia and hypophosphatemia have been observed in patients on prolonged thiazide therapy. Thiazides may also decrease serum PBI levels without evidence of alteration of thyroid function. **USAGE IN PREGNANCY**: Spironolactone or its metabolites may, and hydrochlorothiazide does, cross the placental barrier. Therefore, the use of it in pregnant women requires that the anticipated benefit be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possible other adverse reactions which have been reported in the adult. **NURSING MOTHERS**: Canrenone, a metabolite of spironolactone, and hydrochlorothiazide appear in breast milk. If use of these drugs is deemed essential, an alternative method of infant feeding should be instituted. **ADVERSE REACTIONS**: Gynecomastia is observed not infrequently. Other adverse reactions that have been reported in association with the use of spironolactone are: gastrointestinal smyptoms including cramping and diarrhea; drowsiness, lethargy, headache; maculopapular or erythematous cutaneous eruptions; urticaria; mental confusion; drug fever; ataxia; inability to achieve or maintain erection; irregular menses or amenorrhea; postmenopausal bleeding; hirsutism and deepening of the voice. Carcinoma of the breast has been reported in patients taking spironolactone, but a cause and effect relationship has not been established. Adverse reactions reported in association with the use of thiazides include: **A. Gastrointestinal System**: 1. Anorexia, 2. gastric irritation, 3. nausea, 4. vomiting, 5. cramping, 6. diarrhea, 7. constipation, 8. jaundice (intrahepatic cholestatic jaundice), 9. pancreatitis, 10. sialadenitis. **B. Central Nervous System**: 1. dizziness, 2. vertigo, 3. paresthesia, 4. headache, 5. xanthopsia. **C. Hematologic**: 1. leukopenia, 2. agranulocytosis, 3. thrombocytopenia, 4. aplastic anemia. **D. Cardiovascular**: 1. orthostatic hypotension (may be aggravated by alcohol, barbiturates, or narcotics). **E. Hypersensitivity**: 1. purpura, 2. photosensitivity, 3. rash, 4. urticaria, 5. necrotizing angiitis (vasculitis) (cutaneous vasculitis), 6. fever, 7. anaphylactic reactions, 8. respiratory distress, including pneumonitis. **F. Other**: 1. hyperglycemia, 2. glycosuria, 3. hyperuricemia, 4. muscle spasm, 5. weakness, 6. restlessness, 7. transient blurred vision. Whenever adverse reactions are moderate or severe, hydrochlorothiazide dosage should be reduced or therapy withdrawn.

THYROID TABLETS

INDICATIONS: Thyroid is indicated as replacement or substitution therapy of diminished or absent thyroid function (e.g., cretinism, myxedema, nont